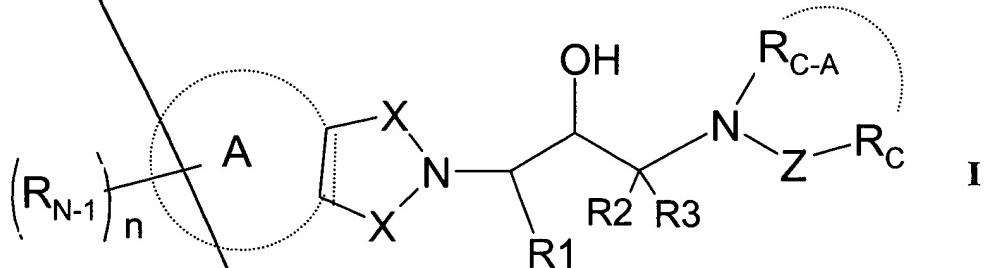


We claim:

1) A disubstituted amine of formula I



where R₁ is:

(I) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, C₁-C₇ alkyl (optionally substituted with C₁-C₃ alkyl and C₁-C₃ alkoxy), -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl, and -OC=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(II) -CH₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(III) -CH₂-CH₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(IV) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(V) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(VI) -(CH₂)_{n1}-(R_{1-aryl}) where n₁ is zero or one and where R_{1-aryl} is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A) C₁-C₆ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(B) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(C) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(D) -F, Cl, -Br or -I,

(F) -C₁-C₆ alkoxy optionally substituted with one, two, or three -F,

(G) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,

(H) -OH,

(I) -C≡N,

(J) C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(K) -CO-(C₁-C₄ alkyl),

(L) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(M) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or

(N) -SO₂-(C₁-C₄ alkyl),

(VII) -(CH₂)_{n1}-(R_{1-heteroaryl}) where n₁ is as defined above and where R_{1-heteroaryl} is selected from the group consisting of:

pyridinyl,

pyrimidinyl,

quinolinyl,

benzothienyl,

indolyl,

indolinyl,

pyridazinyl,

pyrazinyl,

isoquinolyl,

quinazolinyl,
quinoxalinyl,
phthalazinyl,
imidazolyl,
isoxazolyl,
pyrazolyl,
oxazolyl,
thiazolyl,
indolizinyl,
indazolyl,
benzothiazolyl,
benzimidazolyl,
benzofuranyl,
furanyl,
thienyl,
pyrrolyl,
oxadiazolyl,
thiadiazolyl,
triazolyl,
tetrazolyl,
oxazolopyridinyl,
imidazopyridinyl,
isothiazolyl,
naphthyridinyl,
cinnolinyl,
carbazolyl,
beta-carbolinyl,
isochromanyl,
chromanyl,
tetrahydroisoquinolinyl,
isoindolinyl,

isobenzotetrahydrofuranyl,
isobenzotetrahydrothienyl,
isobenzothienyl,
benzoxazolyl,
pyridopyridinyl,
benzotetrahydrofuranyl,
benzotetrahydrothienyl,
purinyl,
benzodioxolyl,
triazinyl,
phenoxyazinyl,
phenothiazinyl,
pteridinyl,
benzothiazolyl,
imidazopyridinyl,
imidazothiazolyl,
dihydrobenzisoxazinyl,
benzisoxazinyl,
benzoxazinyl,
dihydrobenzisothiazinyl,
benzopyranyl,
benzothiopyranyl,
coumarinyl,
isocoumarinyl,
chromonyl,
chromanonyl,
pyridinyl-N-oxide,
tetrahydroquinolinyl
dihydroquinolinyl
dihydroquinolinonyl
dihydroisoquinolinonyl

dihydrocoumarinyl
dihydroisocoumarinyl
isoindolinonyl
benzodioxanyl
benzoxazolinonyl
pyrrolyl N-oxide,
pyrimidinyl N-oxide,
pyridazinyl N-oxide,
pyrazinyl N-oxide,
quinolinyl N-oxide,
indolyl N-oxide,
indolinyl N-oxide,
isoquinolyl N-oxide,
quinazolinyl N-oxide,
quinoxalinyl N-oxide,
phthalazinyl N-oxide,
imidazolyl N-oxide,
isoxazolyl N-oxide,
oxazolyl N-oxide,
thiazolyl N-oxide,
indolizinyl N-oxide,
indazolyl N-oxide,
benzothiazolyl N-oxide,
benzimidazolyl N-oxide,
pyrrolyl N-oxide,
oxadiazolyl N-oxide,
thiadiazolyl N-oxide,
triazolyl N-oxide,
tetrazolyl N-oxide,
benzothiopyranyl S-oxide, and
benzothiopyranyl S,S-dioxide,

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

where the $R_{1\text{-heteraryl}}$ group is bonded to $-(CH_2)_{n_1}-$ by any ring atom of the parent R_N -heteraryl group substituted by hydrogen such that the new bond to the $R_{1\text{-heteraryl}}$ group replaces the hydrogen atom and its bond, where heteraryl is optionally substituted with one, two, three, or four:

- (1) $C_1\text{-}C_6$ alkyl optionally substituted with one, two or three substituents selected from the group consisting of $C_1\text{-}C_3$ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
 - (2) $C_2\text{-}C_6$ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,
 - (3) $C_2\text{-}C_6$ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,
 - (4) -F, Cl, -Br, or -I,
 - (6) $-C_1\text{-}C_6$ alkoxy optionally substituted with one, two, or three -F,
 - (7) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,
 - (8) -OH,
 - (9) -C≡N,
 - (10) $C_3\text{-}C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,
 - (11) -CO-($C_1\text{-}C_4$ alkyl),
 - (12) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
 - (13) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or
 - (14) -SO₂-($C_1\text{-}C_4$ alkyl), with the proviso that when n₁ is zero R_1 -heteraryl is not bonded to the carbon chain by nitrogen, or
 - (VIII) $-(CH_2)_{n_1}\text{-}(R_1\text{-heterocycle})$ where n₁ is as defined above and $R_1\text{-heterocycle}$ is selected from the group consisting of:
- morpholinyl,

thiomorpholinyl,
thiomorpholinyl S-oxide,
thiomorpholinyl S,S-dioxide,
piperazinyl,
homopiperazinyl,
pyrrolidinyl,
pyrrolinyl,
tetrahydropyranyl,
piperidinyl,
tetrahydrofuranyl,
tetrahydrothienyl,
homopiperidinyl,
homomorpholinyl,
homothiomorpholinyl,
homothiomorpholinyl S,S-dioxide,
~~oxazolidinonyl~~,
~~dihydropyrazoly~~,
~~dihydropyrrolyl~~,
~~dihydropyrazinyl~~,
~~dihydropyridinyl~~,
~~dihydropyrimidinyl~~,
~~dihydrofuryl~~,
~~dihydropyranyl~~,
~~tetrahydrothienyl S-oxide~~,
~~tetrahydrothienyl S,S-dioxide~~, and
~~homothiomorpholinyl S-oxide~~,

where the R_1 -heterocycle group is bonded by any atom of the parent R_1 -heterocycle group substituted by hydrogen such that the new bond to the R_1 -heterocycle group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three, or four:

- (1) C₁-C₆ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
- (2) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
- (3) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
- (4) -F, Cl, -Br, or -I,
- (5) C₁-C₆ alkoxy,
- (6) -C₁-C₆ alkoxy substituted with one, two, or three -F,
- (7) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,
- (8) -OH,
- (9) -C≡N,
- (10) C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
- (11) -CO-(C₁-C₄ alkyl),
- (12) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
- (13) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
- (14) -SO₂-(C₁-C₄ alkyl), or
- (15) =O, with the proviso that when n₁ is zero R₁-heterocycle is not bonded to the carbon chain by nitrogen;

where R₂ is:

(I)-H,

(II) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH,

-SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(III) -(CH₂)₀₋₄-R₂₋₁ where R₂₋₁ is R_{1-aryl} or R_{1-heteroaryl} where R_{1-aryl} and R_{1-heteroaryl} are as defined above;

(IV) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(V) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl, or

(VI) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

where R₃ is:

(I)-H,

(II) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH,

-SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(III) -(CH₂)₀₋₄-R₂₋₁ where R₂₋₁ is R_{1-aryl} or R_{1-heteroaryl} where R_{1-aryl} and R_{1-heteroaryl} are as defined above;

(IV) C₂-C₆ alkenyl with one or two double bonds,

(V) C₂-C₆ alkynyl with one or two triple bonds, or

(VI) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

where R₂ and R₃ are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO₂-, and -NR_{N-2-},

where R_{N-2} is selected from the group consisting of:

- (a) -H,
- (b) -C₁-C₆ alkyl optionally substituted with one substituent selected from the group consisting of:
 - (i) -OH, and
 - (ii) -NH₂,
- (c) -C₁-C₆ alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,
- (d) -C₃-C₇ cycloalkyl,
- (e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),
- (f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),
- (g) -C₂-C₆ alkenyl with one or two double bonds,
- (h) -C₂-C₆ alkynyl with one or two triple bonds,
- (i) -C₁-C₆ alkyl chain with one double bond and one triple bond,
- (j) -R_{1-aryl} where R_{1-aryl} is as defined above, and
- (k) -R_{1-heteroaryl} where R_{1-heteroaryl} is as defined above;

where X is independently chosen from the group consisting of:

- C(O)-,
- CH₂-,
- CH₂-CH₂-, and
- CH₂-C(O)-;

wherein in the rings drawn, a dotted line indicates an optional double bond or an optional ring;

wherein ring A is phenyl, cyclohexyl, cyclopentyl, pyridyl, pyrimidinyl, pyrazinyl or is absent; and

where R_{N-1} is selected from the group consisting of:

- (1) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I,

-OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

- (2) -OH,
- (3) -NO₂,
- (4) -F, -Cl, -Br, or -I,
- (5) -CO-OH,
- (6) -C≡N,
- (7) -(CH₂)₀₋₄-CO-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and are selected from the group consisting of:

- (a) -H,
- (b) -C₁-C₆ alkyl optionally substituted with one substituent selected from the group consisting of:
 - (i) -OH, and
 - (ii) -NH₂,
 - (c) -C₁-C₆ alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,
 - (d) -C₃-C₆ cycloalkyl,
 - (e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),
 - (f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),
 - (g) -C₂-C₆ alkenyl with one or two double bonds,
 - (h) -C₂-C₆ alkynyl with one or two triple bonds,
 - (i) -C₁-C₆ alkyl chain with one double bond and one triple bond,
 - (j) -R_{1-aryl} where R_{1-aryl} is as defined above, and
 - (k) -R_{1-heteroaryl} where R_{1-heteroaryl} is as defined above,
- (8) -(CH₂)₀₋₄-CO-(C₁-C₁₂ alkyl),
- (9) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkenyl with one, two, or three double bonds),
- (10) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkynyl with one, two, or three triple bonds),
- (11) -(CH₂)₀₋₄-CO-(C₃-C₇ cycloalkyl),

- (12) $-(CH_2)_{0-4}-CO-R_{1-aryl}$ where R_{1-aryl} is as defined above,
- (13) $-(CH_2)_{0-4}-CO-R_{1-heteroaryl}$ where $R_{1-heteroaryl}$ is as defined above,
- (14) $-(CH_2)_{0-4}-CO-R_{1-heterocycle}$ where $R_{1-heterocycle}$ is as defined above,
- (15) $-(CH_2)_{0-4}-CO-R_{N-4}$ where R_{N-4} is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of: C_1-C_6 alkyl,
- (16) $-(CH_2)_{0-4}-CO-O-R_{N-5}$ where R_{N-5} is selected from the group consisting of:
- (a) C_1-C_6 alkyl,
 - (b) $-(CH_2)_{0-2}-(R_{1-aryl})$ where R_{1-aryl} is as defined above,
 - (c) C_2-C_6 alkenyl containing one, or two double bonds,
 - (d) C_2-C_6 alkynyl containing one, or two triple bonds,
 - (e) C_3-C_7 cycloalkyl, and
 - (f) $-(CH_2)_{0-2}-(R_{1-heteroaryl})$ where $R_{1-heteroaryl}$ is as defined above,
- (17) $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined above,
- (18) $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl),
- (19) $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl),
- (20) $-(CH_2)_{0-4}-SO_2-(C_3-C_7$ cycloalkyl),
- (21) $-(CH_2)_{0-4}-N(H$ or $R_{N-5})-CO-O-R_{N-5}$ where R_{N-5} can be the same or different and is as defined above,
- (22) $-(CH_2)_{0-4}-N(H$ or $R_{N-5})-CO-N(R_{N-5})_2$, where R_{N-5} can be the same or different and is as defined above,

(23) $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$, where R_{N-5} can be the same or different and is as defined above,

(24) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-CO-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as defined above,

(25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(26) $-(CH_2)_{0-4}-R_{N-4}$ where R_{N-4} is as defined above,

(27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$,

(28) $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$ where $R_{N-aryl-1}$ is $-H$ or C_1-C_4 alkyl,

(29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})_2$ where R_{N-5} is as defined above,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$ where R_{N-5} is as defined above,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})_2$ where R_{N-5} is as defined above,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl}$ optionally substituted with one, two, three, four, or five of: $-F$),

(35) C_3-C_7 cycloalkyl,

(36) C_2-C_6 alkenyl with one or two double bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(37) C_2-C_6 alkynyl with one or two triple bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(38) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as described above, and

(39) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl;

10
9
8
7
6
5
4
3
2
1

where n is equal to 0, 1, 2 or 3;

where Z is selected from the group consisting of:

- (A) $-C(O)-$,
- (B) $-S(O)_{1-2-}$,
- (C) $-C(O)-X_{N-1-}$ where X_{N-1} is selected from the group consisting of $-O-$, $-S-$ and $-NR'$ and where R' is as defined above; and
- (D) a single bond;

where R_C is:

(I) C_1-C_{10} alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_6 alkoxy, $-O$ -phenyl, $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, $-OC=O NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, $-S(=O)_{0-2} R_{1-a}$ where R_{1-a} is as defined above, $-NR_{1-a}C=O NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, $-C=O NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, and $-S(=O)_2 NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(II) $-(CH_2)_{0-3-}(C_3-C_8)$ cycloalkyl where cycloalkyl can be optionally substituted with one, two, or three substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_6 alkoxy, $-O$ -phenyl, $-CO-OH$, $-CO-O-(C_1-C_4$ alkyl), and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

- (III) $-(CR_{C-x}R_{C-y})_{0-4-}R_{C-aryl}$ where R_{C-x} and R_{C-y} are
- (A) $-H$,
 - (B) C_1-C_4 alkyl optionally substituted with one or two $-OH$,
 - (C) C_1-C_4 alkoxy optionally substituted with one, two, or three $-F$,
 - (D) $-(CH_2)_{0-4-}C_3-C_7$ cycloalkyl,
 - (E) C_2-C_6 alkenyl containing one or two double bonds,
 - (F) C_2-C_6 alkynyl containing one or two triple bonds,
 - (G) phenyl-,
 - (H) C_0-C_4 alkyl $C(O) NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

and where R_{C-x} and R_{C-y} are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of $-O-$, $-S-$, $-SO_2-$, $-NR_{N-2}-$ and R_{C-aryl} is the same as R_{N-aryl} and where R_{C-aryl} may optionally be substituted with $-C_0-C_4$ alkyl- $C(O)NR_{1-a}R_{1-b}$, C_0-C_4 alkyl $C(O)OR_{1-a}$ where R_{1-a} and R_{1-b} are as defined above,

(IV) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is the same as $R_{N-heteroaryl}$ and R_{C-x} and R_{C-y} are as defined above,

(V) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-aryl}$ where R_{C-aryl} , R_{C-x} and R_{C-y} are as defined above,

(VI) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heteroaryl}$ where R_{C-aryl} , $R_{C-heteroaryl}$, R_{C-x} and R_{C-y} are as defined above,

(VII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-aryl}$ where $R_{C-heteroaryl}$, R_{C-aryl} , R_{C-x} and R_{C-y} are as defined above,

(VIII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$, R_{C-x} and R_{C-y} are as defined above,

(IX) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heterocycle}$ where $R_{C-heterocycle}$ is the same as $R_{1-heterocycle}$, and R_{C-aryl} , R_{C-x} and R_{C-y} are as defined above,

(X) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heterocycle}$ where $R_{C-heteroaryl}$, $R_{C-heterocycle}$, R_{C-x} and R_{C-y} are as defined above,

(XI) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-aryl}$ where $R_{C-heterocycle}$, R_{C-aryl} , R_{C-x} and R_{C-y} are as defined above,

(XII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heteroaryl}$ where $R_{C-heterocycle}$, $R_{C-heteroaryl}$, R_{C-x} and R_{C-y} are as defined above,

(XIII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heterocycle}$ where $R_{C-heterocycle}$, R_{C-x} and R_{C-y} are as defined above,

(XIV) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$ where $R_{C-heterocycle}$, R_{C-x} , and R_{C-y} are as defined above,

(XV) $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$ where R_{C-3} is as defined below and R_{C-1} , R_{C-2} are the same or different and are selected from the group consisting of:

(A) -H,

(B) -C₁-C₆ alkyl, optionally substituted with one, two, or three substituents independently selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(D) C₂-C₆ alkenyl with one, or two double bonds, optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(E) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(F) -(CH₂)₁₋₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(F) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl, optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(G) -(C₁-C₄ alkyl)-R_{C'-aryl} where R_{C'-aryl} is as defined for R_{1-aryl},

(H) -(C₁-C₄ alkyl)-R_{C-heteroaryl} where R_{C-heteroaryl} is as defined above,

(I) -(C₁-C₄ alkyl)-R_{C-heterocycle} where R_{C-heterocycle} is as defined above,

(J) -R_{C-heteroaryl} where R_{C-heteroaryl} is as defined above,

(K) -R_{C-heterocycle} where R_{C-heterocycle} is as defined above,

(M) -(CH₂)₁₋₄-R_{C-4}-(CH₂)₀₋₄-R_{C'-aryl} where R_{C-4} is -O-, -S- or -NR_{C-5-} where R_{C-5} is C₁-C₆ alkyl, and where R_{C'-aryl} is defined above,

(N) -(CH₂)₁₋₄-R_{C-4}-(CH₂)₀₋₄-R_{C-heteroaryl} where R_{C-4} and R_{C-heteroaryl} are as defined above, and

(O) -R_{C'-aryl} where R_{C'-aryl} is as defined above,

and where R_{C-3} is the same or different and is:

(a) -H,

(b) $-C_1-C_6$ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(c) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(d) C_2-C_6 alkynyl with one, or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(e) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(f) $-R_{C'-aryl}$ where R_{C'-aryl} is as defined above,

(g) $-R_{C-heteroaryl}$ where R_{C-heteroaryl} is as defined above,

(h) $-R_{C-heterocycle}$ where R_{C-heterocycle} is as defined above,

(i) $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$ where R_{C'-aryl} is as defined above,

(j) $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$ where R_{C-heteroaryl} is as defined above,

(k) $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$ where R_{C-heterocycle} is as defined above,

(XVI) $-CH(R_{C-aryl})_2$ where R_{C-aryl} are the same or different and are as defined above,

(XVII) $-CH(R_{C-heteroaryl})_2$ where R_{C-heteroaryl} are the same or different and are as defined above,

(XVIII) $-CH(R_{C-aryl})(R_{C-heteroaryl})$ where R_{C-aryl} and R_{C-heteroaryl} are as defined above,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle} where R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle} are as defined above where one carbon of cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with NH, NR_{N-5}, O, or S(=O)₀₋₂, and where cyclopentyl, cyclohexyl, or cycloheptyl can be optionally substituted with one, or two -C₁-C₃ alkyl, -F, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, =O, or -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(XX) C₂-C₁₀ alkenyl containing one or two double bonds optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(XXI) C₂-C₁₀ alkynyl containing one, or two triple bonds optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(XXI) -(CH₂)₀₋₁-CHR_{C-6}-(CH₂)₀₋₁-R_{C-aryl} where R_{C-aryl} is as defined above and R_{C-6} is -(CH₂)₀₋₆-OH,

(XXII) -(CH₂)₀₋₁-CHR_{C-6}-(CH₂)₀₋₁-R_{C-heteroaryl} where R_{C-heteroaryl} and R_{C-6} is as defined above,

(XXIII) -CH(-R_{C-aryl} or R_{C-heteroaryl})-CO-O(C₁-C₄ alkyl) where R_{C-aryl} and R_{C-heteroaryl} are as defined above,

(XXIV) -CH(-CH₂-OH)-CH(-OH)-phenyl-NO₂,

(XXV) (C₁-C₆ alkyl)-O-(C₁-C₆ alkyl)-OH,

(XXVII) -CH₂-NH-CH₂-CH(-O-CH₂-CH₃)₂, or

(XXVIII) - (CH₂)₀₋₆-C(=NR_{1-a})(NR_{1-a}R_{1-b}) where R_{1-a} and R_{1-b} are as defined above,

where R_{C-A} is H, C₁ - C₁₀ alkyl, C₂ - C₁₀ alkenyl and alkynyl, phenyl, C₁ - C₄ alkyl-R_{N-aryl}, C₁ - C₄ alkyl-R_{N-heteroaryl}, C₁ - C₄ alkyl-C₃-C₇ cycloalkyl, or C₁ - C₄ alkyl-R_{1-heterocycle}, wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -

SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -C(O)O-R_{1-a}, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H, C₁-C₆ alkyl or phenyl;

where R_{C-A}, -Z-R_C, and the nitrogen atom to which they attach may cyclize to form a ring or fused rings chosen from the group consisting of 5-8 membered heterocyclics having up to 2 heteroatoms in addition to the ring nitrogen defined above chosen from the group consisting of N, O, and S, which may optionally be fused with one, or two phenyl, pyridyl, cyclohexyl, piperidinyl or morpholinyl,

where the ring or fused rings may optionally have one, two, or three substituents independently chosen from the group of:

(1) C₁-C₆ alkyl,

C₂-C₆ alkenyl with one or two double bonds, or

C₂-C₆ alkynyl with one or two triple bonds, wherein each may be optionally substituted with one, two, or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(2) -F, Cl, -Br, or -I,

(3) -C₁-C₆ alkoxy optionally substituted with one, two, or three -F,

(4) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,

(5) -OH,

(6) -C≡N,

(7) =O (oxo),

(8) -CO-(C₁-C₄ alkyl),

(9) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or

(10) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

or a pharmaceutically acceptable salt thereof.

2. A disubstituted amine of claim 1, wherein R₁ is:

-(CH₂)₀₋₁-(R₁-aryl), or

-(CH₂)_{n1}-(R₁-heteroaryl).

3. A disubstituted amine of claim 2, wherein R₁ is:

$-(CH_2)-(R_1\text{-aryl})$, or
 $-(CH_2)-(R_1\text{-heteroaryl})$.

4. A disubstituted amine of claim 3, wherein R₁ is -(CH₂)-(R_{1-aryl}) where R_{1-aryl} is phenyl.

5. A disubstituted amine of claim 4, wherein R₁ is substituted with two -F.

6. A disubstituted amine of claim 5, wherein the -F substitutions is on the -3 and -5 positions.

7. A disubstituted amine of claim 1, wherein R₂ and R₃ are both -H.

8. A disubstituted amine of claim 1, wherein R_C is:

 - C₁-C₈ alkyl,
 - (CH₂)₀₋₃-(C₃-C₇) cycloalkyl,
 - (CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl},
 - (CR_{C-x}R_{C-y})₀₋₄-R_{C-heteroaryl},
 - (CR_{C-x}R_{C-y})₀₋₄-R_{C-heterocycle}, or
 - cyclopentyl or -cyclohexyl ring fused to R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle}.

9. A disubstituted amine of claim 8, wherein R_C is:

 - (CH₂)₀₋₃-(C₃-C₇) cycloalkyl,
 - (CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl},
 - (CR_{C-x}R_{C-y})₀₋₄-R_{C-heteroaryl},
 - (CR_{C-x}R_{C-y})₀₋₄-R_{C-heterocycle},
 - cyclopentyl or -cyclohexyl ring fused to a R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle}.

10. A disubstituted amine of claim 9, wherein R_C is:

 - (CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl},
 - (CR_{C-x}R_{C-y})₀₋₄-R_{C-heteroaryl},
 - cyclopentyl or -cyclohexyl ring fused to a R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle}.

11. A disubstituted amine of claim 10, wherein R_C is:

$-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ where R_{C-aryl} is phenyl.

12. A disubstituted amine of claim 11, wherein said phenyl is substituted in the 3-position or 3,5-positions.

13. A disubstituted amine of claim 1, wherein R_{C-A} is:

-methyl, or

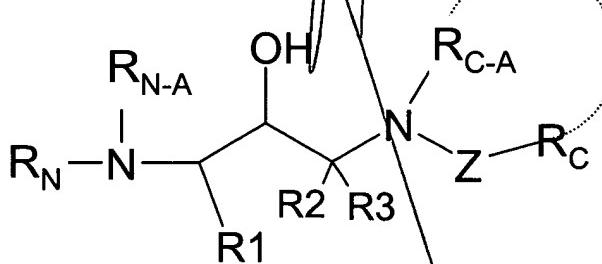
-ethyl.

14. A disubstituted amine of claim 1, wherein Z is:

$-C(O)-$, or

$-C(O)-X_{N-1}-$ where X_{N-1} is selected from the group consisting of $-O-$, $-S-$ and $-NR'$.

15. A disubstituted amine of formula II



where R_1 is:

(I) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, C_1-C_7 alkyl (optionally substituted with C_1-C_3 alkyl and C_1-C_3 alkoxy), $-F$, $-Cl$, $-Br$, $-I$, $-OH$,

-SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl, and
-OC=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(II) -CH₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(III) -CH₂-CH₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(IV) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(V) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(VI) -(CH₂)_{n1}-(R_{1-aryl}) where n₁ is zero or one and where R_{1-aryl} is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A) C₁-C₆ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(B) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(C) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(D) -F, Cl, -Br or -I,

(E) -C₁-C₆ alkoxy optionally substituted with one, two, or three -F,

(G) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,

(H) -OH,

(I) -C≡N,

(J) C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(K) -CO-(C₁-C₄ alkyl),

(L) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(M) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or

(N) -SO₂-(C₁-C₄ alkyl),

(VII) -(CH₂)_{n1}-(R_{1-heteroaryl}) where n₁ is as defined above and where R₁₋ heteroaryl is selected from the group consisting of:

pyridinyl,

pyrimidinyl,

quinolinyl,

benzothienyl,

indolyl,

indolinyl,

pyridazinyl,

pyrazinyl,

isoquindinyl,

quinazolinyl,

quinoxaliny,

phthalazinyl,

imidazolyl,

isoxazolyl,

pyrazolyl,

oxazolyl,

thiazolyl,

indolizinyl,

indazolyl,

benzothiazolyl,

benzimidazolyl,

benzofuranyl,

furanyl,
thienyl,
pyrrolyl,
oxadiazolyl,
thiadiazolyl,
triazolyl,
tetrazolyl,
oxazolopyridinyl,
imidazopyridinyl,
isothiazolyl,
naphthyridinyl,
cinnolinyl,
carbazolyl,
beta-carbolinyl,
isochromanyl,
chromanyl,
tetrahydroisoquinolinyl,
isoindolinyl,
isobenzotetrahydrofuranyl,
isobenzotetrahydrothienyl,
isobenzothienyl,
benzoxazolyl,
pyridopyridinyl,
benzotetrahydrofuranyl,
benzotetrahydrothienyl,
purinyl,
benzodioxolyl,
triazinyl,
phenoxyazinyl,
phenothiazinyl,
pteridinyl,

benzothiazolyl,
imidazopyridinyl,
imidazothiazolyl,
dihydrobenzisoxazinyl,
benzisoxazinyl,
benzoxazinyl,
dihydrobenzisothiazinyl,
benzopyranyl,
benzothiopyranyl,
coumarinyl,
isocoumarinyl,
chromonyl,
chromanonyl,
pyridinyl-N-oxide,
tetrahydroquinolinyl
dihydroquinolinyl
~~dihydroquinolinonyl~~
dihydroisoquinolinonyl
dihydrocoumarinyl
dihydroisocoumarinyl
isoindolinonyl
benzdioxanyl
benzoxazolinonyl
pyrrolyl N-oxide,
pyrimidinyl N-oxide,
pyridazinyl N-oxide,
pyrazinyl N-oxide,
quinolinyl N-oxide,
indolyl N-oxide,
indolinyl N-oxide,
isoquinolyl N-oxide,

quinazolinyl N-oxide,
quinoxalinyl N-oxide,
phthalazinyl N-oxide,
imidazolyl N-oxide,
isoxazolyl N-oxide,
oxazolyl N-oxide,
thiazolyl N-oxide,
indolizinyl N-oxide,
indazolyl N-oxide,
benzothiazolyl N-oxide,
benzimidazolyl N-oxide,
pyrrolyl N-oxide,
oxadiazolyl N-oxide,
thiadiazolyl N-oxide,
triazolyl N-oxide,
tetrazolyl N-oxide,
benzothiopyranyl S-oxide, and
benzothiopyranyl S,S-dioxide,

where the $R_{1\text{-heteraryl}}$ group is bonded to $-\text{CH}_2\text{n}_1-$ by any ring atom of the parent R_N -heteraryl group substituted by hydrogen such that the new bond to the $R_{1\text{-heteraryl}}$ group replaces the hydrogen atom and its bond, where heteraryl is optionally substituted with one, two, three, or four:

(1) $C_1\text{-}C_6$ alkyl optionally substituted with one, two or three substituents selected from the group consisting of $C_1\text{-}C_3$ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(2) $C_2\text{-}C_6$ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,

(3) $C_2\text{-}C_6$ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -

Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

- (4) -F, Cl, -BR, or -I,
- (6) -C₁-C₆ alkoxy optionally substituted with one, two, or three -F,
- (7) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,
- (8) -OH,
- (9) -C≡N,
- (10) C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
- (11) -CO-(C₁-C₄ alkyl),
- (12) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
- (13) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or
- (14) -SO₂-(C₁-C₄ alkyl), with the proviso that when n₁ is zero R_{1-heteraryl} is not bonded to the carbon chain by nitrogen, or

(VIII) -(CH₂)_{n1}-(R_{1-heterocycle}) where n₁ is as defined above and R_{1-heterocycle} is selected from the group consisting of:

- morpholinyl,
- thiomorpholinyl,
- thiomorpholinyl S-oxide,
- thiomorpholinyl S,S-dioxide,
- piperazinyl,
- homopiperazinyl,
- pyrrolidinyl,
- pyrrolinyl,
- tetrahydropyranyl,
- piperidinyl,
- tetrahydrofuranyl,
- tetrahydrothienyl,
- homopiperidinyl,
- homomorpholinyl,

homothiomorpholinyl,
homothiomorpholinyl S,S-dioxide,
oxazolidinonyl,
dihydropyrazolyl,
dihydropyrrolyl,
dihydropyrazinyl,
dihydropyridinyl,
dihydropyrimidinyl,
dihydrofuryl,
dihdropyranyl,
tetrahydrothienyl S-oxide,
tetrahydrothienyl S,S-dioxide, and
homothiomorpholinyl S-oxide,

where the R₁-heterocycle group is bonded by any atom of the parent R₁-heterocycle group substituted by hydrogen such that the new bond to the R₁-heterocycle group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three, or four:

(1) C₁-C₆ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(2) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(3) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(4) -F, Cl, -Br, or -I,

(5) C₁-C₆ alkoxy,

(6) -C₁-C₆ alkoxy substituted with one, two, or three -F,

(7) $-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined below,

(8) $-OH$,

(9) $-C\equiv N$,

(10) C_3-C_7 cycloalkyl, optionally substituted with one, two

or three substituents selected from the group consisting of $-F$, $-Cl$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are $-H$ or C_1-C_6 alkyl,

(11) $-CO-(C_1-C_4$ alkyl),

(12) $-SO_2-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined

above,

(13) $-CO-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined

above,

(14) $-SO_2-(C_1-C_4$ alkyl), or

(15) $=O$, with the proviso that when n_1 is zero $R_{1-heterocycle}$ is not bonded to the carbon chain by nitrogen;

where R_2 is:

(I) H ,

(II) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$,

$-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(III) $-(CH_2)_{0-4}-R_{2-1}$ where R_{2-1} is R_{1-aryl} or $R_{1-heteroaryl}$ where R_{1-aryl} and $R_{1-heteroaryl}$ are as defined above;

(IV) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of $-F$, $-Cl$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are $-H$ or C_1-C_6 alkyl,

(V) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of $-F$, $-Cl$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are $-H$ or C_1-C_6 alkyl, or

(VI) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of $-F$, $-Cl$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are $-H$ or C_1-C_6 alkyl,

where R₃ is selected from the group consisting of:

(I) -H,

(II) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(III) -(CH₂)₀₋₄-R₂₋₁ where R₂₋₁ is R_{1-aryl} or R_{1-heteroaryl} where R_{1-aryl} and R_{1-heteroaryl} are as defined above;

(IV) C₂-C₆ alkenyl with one or two double bonds,

(V) C₂-C₆ alkynyl with one or two triple bonds, or

(VI) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

and where R₂ and R₃ are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO₂-, and -NR_{N-2-},

where R_{N-2} is selected from the group consisting of:

(a) -H,

(b) -C₁-C₆ alkyl optionally substituted with one

substituent selected from the group consisting of:

(i) -OH, and

(ii) -NH₂,

(c) -C₁-C₆ alkyl optionally substituted with one to

three -F, -Cl, -Br, or -I,

(d) -C₃-C₇ cycloalkyl,

(e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),

(f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),

(g) -C₂-C₆ alkenyl with one or two double bonds,

(h) -C₂-C₆ alkynyl with one or two triple bonds,

triple bond,

(i) -C₁-C₆ alkyl chain with one double bond and one

(j) -R_{1-aryl} where R_{1-aryl} is as defined above, and

(k) -R_{1-heteroaryl} where R_{1-heteroaryl} is as defined above;

where R_N is:

(I) R_{N-1}-X_N- where X_N is selected from the group consisting of:

(A) -CO-,

(B) -SO₂-,

(C) -(CR'R'')₁₋₆ where R' and R'' are the same or different and are -H or C₁-C₄ alkyl,

(D) -CO-(CR'R'')₁₋₆-X_{N-1} where X_{N-1} is selected from the group consisting of -O-, -S- and -NR'- and where R' and R'' are as defined above, and

(E) a single bond;

where R_{N-1} is selected from the group consisting of:

(A) R_{N-aryl} where R_{N-aryl} is phenyl, 1-naphthyl, 2-naphthyl, tetralinyl, indanyl, or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl, or dihydronaphthyl optionally substituted with one, two or three of the following substituents which can be the same or different and are:

(1) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(2) -OH,

(3) -NO₂,

(4) -F, -Cl, -Br, or -I,

(5) -CO-OH,

(6) -C≡N,

(7) -(CH₂)₀₋₄-CO-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and are selected from the group consisting of:

- (a) -H,
(b) -C₁-C₆ alkyl optionally substituted with one substituent selected from the group consisting of:
(i) -OH, and
(ii) -NH₂,
(c) -C₁-C₆ alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,

triple bond,

double bonds),

triple bonds),

(d) -C₃-C₇ cycloalkyl,
(e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),
(f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),
(g) -C₂-C₆ alkenyl with one or two double bonds,
(h) -C₂-C₆ alkynyl with one or two triple bonds,
(i) -C₁-C₆ alkyl chain with one double bond and one triple bond,
(j) -R₁-aryl where R₁-aryl is as defined above, and
(k) -R₁-heteroaryl where R₁-heteroaryl is as defined above,
(8) -(CH₂)₀₋₄-CO-(C₁-C₁₂ alkyl),
(9) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkenyl with one, two or three double bonds),
(10) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkynyl with one, two or three triple bonds),
(11) -(CH₂)₀₋₄-CO-(C₃-C₇ cycloalkyl),
(12) -(CH₂)₀₋₄-CO-R₁-aryl where R₁-aryl is as defined above,
(13) -(CH₂)₀₋₄-CO-R₁-heteroaryl where R₁-heteroaryl is as defined above,
(14) -(CH₂)₀₋₄-CO-R₁-heterocycle where R₁-heterocycle is as defined above,
(15) -(CH₂)₀₋₄-CO-R_{N-4} where R_{N-4} is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is

optionally substituted with one, two, three, or four of: C₁-C₆ alkyl,

(16) -(CH₂)₀₋₄-CO-O-R_{N-5} where R_{N-5} is selected from the group consisting of:

(a) C₁-C₆ alkyl,

(b) -(CH₂)₀₋₂-(R_{1-aryl}) where R_{1-aryl} is as defined above,

(c) C₂-C₆ alkenyl containing one or two double bonds,

(d) C₂-C₆ alkynyl containing one or two triple bonds,

(e) C₃-C₇ cycloalkyl,

(f) -(CH₂)₀₋₂-(R_{1-heteroaryl}) where R_{1-heteroaryl} is as defined above,

(17) -(CH₂)₀₋₄-SO₂-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined above,

(18) -(CH₂)₀₋₄-SO-(C₁-C₈ alkyl),

(19) -(CH₂)₀₋₄-SO₂(C₁-C₁₂ alkyl),

(20) -(CH₂)₀₋₄-SO₂(C₃-C₇ cycloalkyl),

(21) -(CH₂)₀₋₄-N(H or R_{N-5})-CO-O-R_{N-5} where R_{N-5} can be the same or different and is as defined above,

(22) -(CH₂)₀₋₄-N(H or R_{N-5})-CO-N(R_{N-5})₂, where R_{N-5} can be the same or different and is as defined above,

(23) -(CH₂)₀₋₄-N-CS-N(R_{N-5})₂, where R_{N-5} can be the same or different and is as defined above,

(24) -(CH₂)₀₋₄-N(-H or R_{N-5})-CO-R_{N-2} where R_{N-5} and R_{N-2} can be the same or different and are as defined above,

(25) -(CH₂)₀₋₄-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(26) -(CH₂)₀₋₄-R_{N-4} where R_{N-4} is as defined above,

(27) -(CH₂)₀₋₄-O-CO-(C₁-C₆ alkyl),

- (28) $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$ where $R_{N-aryl-1}$ is $-H$ or C_1-C_4 alkyl,
- (29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$ where R_{N-5} is as defined above,
- (30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$ where R_{N-5} is as defined above,
- (31) $-(CH_2)_{0-4}-O-(R_{N-5})_2$ where R_{N-5} is as defined above,
- (32) $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$ where R_{N-5} is as defined above,
- (33) $-(CH_2)_{0-4}-S-(R_{N-5})_2$ where R_{N-5} is as defined above,
- (34) $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with one, two, three, four, or five $-F$),
- (35) C_3-C_7 cycloalkyl,
- (36) C_2-C_6 alkenyl with one or two double bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,
- (37) C_2-C_6 alkynyl with one or two triple bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,
- (38) $-(CH_2)_{0-4}-N(-H$ or $R_{N-5})-SO_2-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as described above, or
- (39) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl,
- (B) $-R_{N-heteroaryl}$, where $R_{N-heteroaryl}$ is selected from the group as defined above in $R_{1-heteroaryl}$ and where the $R_{N-heteroaryl}$ group is bonded by any atom of the parent $R_{N-heteroaryl}$ group substituted by hydrogen such that the new bond to the $R_{N-heteroaryl}$ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four of:
- (1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

- (2) -OH,
- (3) -NO₂,
- (4) -F, -Cl, -Br, or -I,
- (5) -CO-OH,
- (6) -C≡N,
- (7) -(CH₂)₀₋₄-CO-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and are selected from the group consisting of:

(a) -H,
 (b) -C₁-C₆ alkyl optionally substituted with one substituent selected from the group consisting of:
 (i) -OH, and
 (ii) -NH₂,
 (c) -C₁-C₆ alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,
 (d) -C₃-C₇ cycloalkyl,
 (e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),
 (f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),
 (g) -C₃-C₆ alkenyl with one or two double bonds,
 (h) -C₂-C₆ alkynyl with one or two triple bonds,
 (i) -C₁-C₆ alkyl chain with one double bond and one triple bond,
 (j) -R_{1-aryl} where R_{1-aryl} is as defined above, and
 (k) -R_{1-heteroaryl} where R_{1-heteroaryl} is as defined above,
 (8) -(CH₂)₀₋₄-CO-(C₁-C₁₂ alkyl),
 (9) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkenyl with one, two, or three double bonds),
 (10) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkynyl with one, two, or three triple bonds),
 (11) -(CH₂)₀₋₄-CO-(C₃-C₇ cycloalkyl),
 (12) -(CH₂)₀₋₄-CO-R_{1-aryl} where R_{1-aryl} is as defined above,

- (13) $-(CH_2)_{0-4}-CO-R_{1-heteroaryl}$ where $R_{1-heteroaryl}$ is as defined above,
- (14) $-(CH_2)_{0-4}-CO-R_{1-heterocycle}$ where $R_{1-heterocycle}$ is as defined above,
- (15) $-(CH_2)_{0-4}-CO-R_{N-4}$ where R_{N-4} is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of: C_1-C_6 alkyl,
- (16) $-(CH_2)_{0-4}-CO-O-R_{N-5}$ where R_{N-5} is selected from the group consisting of:
- (a) C_1-C_6 alkyl,
 - (b) $-(CH_2)_{0-2}-(R_{1-aryl})$ where R_{1-aryl} is as defined above,
 - (c) C_2-C_6 alkenyl containing one or two double bonds,
 - (d) C_2-C_6 alkynyl containing one or two triple bonds,
 - (e) C_3-C_7 cycloalkyl, and
 - (f) $-(CH_2)_{0-2}-(R_{1-heteroaryl})$ where $R_{1-heteroaryl}$ is as defined above,
- (17) $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined above,
- (18) $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl),
- (19) $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl),
- (20) $-(CH_2)_{0-4}-SO_2-(C_3-C_7$ cycloalkyl),
- (21) $-(CH_2)_{0-4}-N(H$ or $R_{N-5})-CO-O-R_{N-5}$ where R_{N-5} can be the same or different and is as defined above,
- (22) $-(CH_2)_{0-4}-N(H$ or $R_{N-5})-CO-N(R_{N-5})_2$, where R_{N-5} can be the same or different and is as defined above,

(23) $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$, where R_{N-5} can be the same or different and is as defined above,

(24) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-CO-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as defined above,

(25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(26) $-(CH_2)_{0-4}-R_{N-4}$ where R_{N-4} is as defined above,

(27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$,

(28) $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$ where $R_{N-aryl-1}$ is $-H$ or C_1-C_4 alkyl,

(29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})_2$ where R_{N-5} is as defined above,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$ where R_{N-5} is as defined above,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})_2$ where R_{N-5} is as defined above,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl}$ optionally substituted with one, two, three, four, or five of $-F$),

(35) C_3-C_7 cycloalkyl,

(36) C_2-C_6 alkenyl with one or two double bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(37) C_2-C_6 alkynyl with one or two triple bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, or

(38) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as described above,

(39) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl,

(C) $R_{N-aryl}-W-R_{N-aryl}$,

(D) $R_{N\text{-aryl}}-W-R_{N\text{-heteroaryl}}$,
 (E) $R_{N\text{-aryl}}-W-R_{N-1\text{-heterocycle}}$, where $R_{N-1\text{-heterocycle}}$ is the same as R_1 -heterocycle, as defined above,

- (F) $R_{N\text{-heteroaryl}}-W-R_{N\text{-aryl}}$,
- (G) $R_{N\text{-heteroaryl}}-W-R_{N\text{-heteroaryl}}$,
- (H) $R_{N\text{-heteroaryl}}-W-R_1\text{-heterocycle}$,
- (I) $R_1\text{-heterocycle}-W-R_{N\text{-aryl}}$,
- (J) $R_1\text{-heterocycle}-W-R_{N\text{-heteroaryl}}$, and
- (K) $R_1\text{-heterocycle}-W-R_1\text{-heterocycle}$,

where W is

- (1) $-(CH_2)_{0-4}-$,
- (2) $-O-$,
- (3) $-S(O)_{0-2}-$,
- (4) $-N(R_{N-5})-$ where R_{N-5} is as defined above, or
- (5) $-CO-$;

(II) $-CO-(C_1-C_{10}\text{ alkyl})$ where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

- (A) $-OH$,
- (B) $-C_1-C_6\text{ alkoxy}$,
- (C) $-C_1-C_6\text{ thioalkoxy}$,
- (D) $-CO-O-R_{N-8}$ where R_{N-8} is $-H$, C_1-C_6 alkyl or $-phenyl$,
- (E) $-CO-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different

and are as defined above,

- (F) $-CO-R_{N-4}$ where R_{N-4} is as defined above,
- (G) $-SO_2-(C_1-C_8\text{ alkyl})$,
- (H) $-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different

and are as defined above,

- (I) $-NH-CO-(C_1-C_6\text{ alkyl})$,
- (J) $-NH-CO-O-R_{N-8}$ where R_{N-8} is as defined above,
- (K) $-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and

are as defined above,

- (L) -R_{N-4} where R_{N-4} is as defined above,
(M) -O-CO-(C₁-C₆ alkyl),
(N) -O-CO-NR_{N-8}R_{N-8} where R_{N-8} are the same or different and are
as defined above,
- (O) -O-(C₁-C₅ alkyl)-COOH,
(P) -O-(C₁-C₆ alkyl optionally substituted with one, two, or three
-F, -Cl, -Br, or -I),
(Q) -NH-SO₂-(C₁-C₆ alkyl), and
(R) -F, or -Cl,
(III) -CO-(C₁-C₆ alkyl)-O-(C₁-C₆ alkyl) where alkyl is optionally
substituted with one, two, or three substituents selected from the group consisting of:
(A) -OH,
(B) -C₁-C₆ alkoxy,
(C) -C₁-C₆ thioalkoxy,
(D) -CO-O-R_{N-8} where R_{N-8} is -H, C₁-C₆ alkyl or -phenyl,
(E) -CO-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different
and are as defined above,
(F) -CO-R_{N-4} where R_{N-4} is as defined above,
(G) -SO₂-(C₁-C₈ alkyl),
(H) -SO₂-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different
and are as defined above,
(I) -NH-CO-(C₁-C₆ alkyl),
(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,
(K) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and
are as defined above,
(L) -R_{N-4} where R_{N-4} is as defined above,
(M) -O-CO-(C₁-C₆ alkyl),
(N) -O-CO-NR_{N-8}R_{N-8} where the R_{N-8}s are the same or different
and are as defined above,
(O) -O-(C₁-C₅ alkyl)-COOH,

(P) $-\text{O}-(\text{C}_1\text{-}\text{C}_6 \text{ alkyl}$ optionally substituted with one, two, or three
 $-\text{F}, -\text{Cl}, -\text{Br}, \text{ or } -\text{I}),$

(Q) $-\text{NH}-\text{SO}_2-(\text{C}_1\text{-}\text{C}_6 \text{ alkyl}),$ and

(R) $-\text{F}, \text{ or } -\text{Cl},$

(IV) $-\text{CO}-(\text{C}_1\text{-}\text{C}_6 \text{ alkyl})-\text{S}-(\text{C}_1\text{-}\text{C}_6 \text{ alkyl})$ where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

(A) $-\text{OH},$

(B) $-\text{C}_1\text{-}\text{C}_6 \text{ alkoxy},$

(C) $-\text{C}_1\text{-}\text{C}_6 \text{ thioalkoxy},$

(D) $-\text{CO}-\text{O}-\text{R}_{\text{N}-8}$ where $\text{R}_{\text{N}-8}$ is as defined above,

(E) $-\text{CO}-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$ where $\text{R}_{\text{N}-2}$ and $\text{R}_{\text{N}-3}$ are the same or different

and are as defined above,

(F) $-\text{CO}-\text{R}_{\text{N}-4}$ where $\text{R}_{\text{N}-4}$ is as defined above,

(G) $-\text{SO}_2-(\text{C}_1\text{-}\text{C}_8 \text{ alkyl}),$

(H) $-\text{SO}_2-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$ where $\text{R}_{\text{N}-2}$ and $\text{R}_{\text{N}-3}$ are the same or different

and are as defined above,

(I) $-\text{NH}-\text{CO}-(\text{C}_1\text{-}\text{C}_6 \text{ alkyl}),$

(J) $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N}-8}$ where $\text{R}_{\text{N}-8}$ is as defined above,

(K) $-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$ where $\text{R}_{\text{N}-2}$ and $\text{R}_{\text{N}-3}$ are the same or different and

are as defined above,

(L) $-\text{R}_{\text{N}-4}$ where $\text{R}_{\text{N}-4}$ is as defined above,

(M) $-\text{O}-\text{CO}-(\text{C}_1\text{-}\text{C}_6 \text{ alkyl}),$

(N) $-\text{O}-\text{CO}-\text{NR}_{\text{N}-8}\text{R}_{\text{N}-8}$ where $\text{R}_{\text{N}-8}$ are the same or different and are

as defined above,

(O) $-\text{O}-(\text{C}_1\text{-}\text{C}_5 \text{ alkyl})-\text{COOH},$

(P) $-\text{O}-(\text{C}_1\text{-}\text{C}_6 \text{ alkyl}$ optionally substituted with one, two, or three
 $-\text{F}, -\text{Cl}, -\text{Br}, \text{ or } -\text{I}),$

(Q) $-\text{NH}-\text{SO}_2-(\text{C}_1\text{-}\text{C}_6 \text{ alkyl}),$ and

(R) $-\text{F}, \text{ or } -\text{Cl},$

(V) $-\text{CO}-\text{CH}(-(\text{CH}_2)_{0-2}-\text{O}-\text{R}_{\text{N}-10})-(\text{CH}_2)_{0-2}-\text{R}_{\text{N-aryl}}/\text{R}_{\text{N-heteroaryl}}$ where $\text{R}_{\text{N-aryl}}$
 and $\text{R}_{\text{N-heteroaryl}}$ are as defined above, where $\text{R}_{\text{N}-10}$ is selected from the group consisting of:

- (A) -H,
(B) C₁-C₆ alkyl,
(C) C₃-C₇ cycloalkyl,
(D) C₂-C₆ alkenyl with one double bond,
(E) C₂-C₆ alkynyl with one triple bond,
(F) R₁-aryl where R₁-aryl is as defined above, and
(G) R_{N-heteroaryl} where R_{N-heteroaryl} is as defined above, or

(VI) -CO-(C₃-C₈ cycloalkyl) where alkyl is optionally substituted with one

or two substituents selected from the group consisting of:

- (A) -(CH₂)₀₋₄-OH,
(B) -(CH₂)₀₋₄-C₁-C₆ alkoxy,
(C) -(CH₂)₀₋₄-C₁-C₆ thioalkoxy,
(D) -(CH₂)₀₋₄-CO-O-R_{N-8} where R_{N-8} is -H, C₁-C₆ alkyl or -phenyl,
(E) -(CH₂)₀₋₄-CO-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and are as defined above,
(F) -(CH₂)₀₋₄-CO-R_{N-4} where R_{N-4} is as defined above,
(G) -(CH₂)₀₋₄-SO₂-(C₁-C₈ alkyl),
(H) -(CH₂)₀₋₄-SO₂-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and are as defined above,
(I) -(CH₂)₀₋₄-NH-CO-(C₁-C₆ alkyl),
(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,
(K) -(CH₂)₀₋₄-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and are as defined above,
(L) -(CH₂)₀₋₄-R_{N-4} where R_{N-4} is as defined above,
(M) -O-CO-(C₁-C₆ alkyl),
(N) -O-CO-NR_{N-8}R_{N-8} where R_{N-8} are the same or different and are as defined above,
(O) -O-(C₁-C₅ alkyl)-COOH,

- (P) -O-(C₁-C₆ alkyl optionally substituted with one, two, or three -F, -Cl, -Br, or -I),
- (Q) -NH-SO₂-(C₁-C₆ alkyl), and
- (R) -F, or -Cl;

where R_{N-A} is selected from the group consisting of H, C₁ - C₁₀ alkyl, C₂ - C₁₀ alkenyl and alkynyl, phenyl, C₁ - C₄ alkyl-R_{N-aryl}, C₁ - C₄ alkyl-R_{N-heteroaryl}, C₁ - C₄ alkyl-C₃-C₇ cycloalkyl and C₁ - C₄ alkyl-R_{1-heterocycle}, wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -C(O)O-R_{1-a}, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H, C₁-C₆ alkyl or phenyl;

where Z is selected from the group consisting of:

(A) -C(O)-,

(B) -S(O)₁₋₂-,

(C) -C(O)-X_{N-1}- where X_{N-1} is selected from the group consisting of -O-, -S- and -NR'- and where R' is as defined above; and

(D) a single bond;

where R_C is:

(I)-C₁-C₁₀ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O-phenyl, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -OC=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -S(=O)₀₋₂ R_{1-a} where R_{1-a} is as defined above, -NR_{1-a}C=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -C=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, and -S(=O)₂ NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(II) -(CH₂)₀₋₃-(C₃-C₈) cycloalkyl where cycloalkyl can be optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O-phenyl, -CO-OH, -CO-O-(C₁-C₄ alkyl), and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

- (III) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ where R_{C-x} and R_{C-y} are
- (A) -H,
 - (B) C₁-C₄ alkyl optionally substituted with one, or two -OH,
 - (C) C₁-C₄ alkoxy optionally substituted with one, two, or three -F,
 - (D) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl,
 - (E) C₂-C₆ alkenyl containing one or two double bonds,
 - (F) C₂-C₆ alkynyl containing one or two triple bonds,
 - (G) phenyl-, or
 - (A) C₀-C₄ alkylC(O) NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

and where R_{C-x} and R_{C-y} are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO₂-, -NR_{N-2}- and R_{C-aryl} where R_{C-aryl} is the same as R_{N-aryl} and where R_{C-aryl} may optionally be substituted with -C₀-C₄ alkyl-C(O) NR_{1-a}R_{1-b}, C₀-C₄ alkylC(O) OR_{1-a} where R_{1-a} and R_{1-b} are as defined above,

(IV) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ where R_{C-heteroaryl} is the same as R_{N-heteroaryl} and R_{C-x} and R_{C-y} are as defined above,

(V) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-aryl}$ where R_{C-aryl}, R_{C-x} and R_{C-y} are as defined above,

(VI) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heteroaryl}$ where R_{C-aryl}, R_{C-heteroaryl}, R_{C-x} and R_{C-y} are as defined above,

(VII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-aryl}$ where R_{C-heteroaryl}, R_{C-aryl}, R_{C-x} and R_{C-y} are as defined above,

(VIII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heteroaryl}$ where R_{C-heteroaryl}, R_{C-x} and R_{C-y} are as defined above,

(IX) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heterocycle}$ where R_{C-heterocycle} is the same as R_{1-heterocycle}, and where R_{C-aryl}, R_{C-x} and R_{C-y} are as defined above,

(X) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heterocycle}$ where R_{C-heteroaryl}, R_{C-heterocycle}, R_{C-x} and R_{C-y} are as defined above,

(XI) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-aryl}$ where $R_{C-heterocycle}$, R_{C-aryl} , R_{C-x} and R_{C-y} are as defined above,

(XII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heteroaryl}$ where $R_{C-heterocycle}$, $R_{C-heteroaryl}$, R_{C-x} and R_{C-y} are as defined above,

(XIII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heterocycle}$ where $R_{C-heterocycle}$, R_{C-x} and R_{C-y} are as defined above,

(XIV) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$ where $R_{C-heterocycle}$, R_{C-x} and R_{C-y} are as defined above,

(XV) $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$ where R_{C-3} is as defined below and R_{C-1} , R_{C-2} are the same or different and are selected from the group consisting of:

(A) -H,

(B) $-C_1-C_6$ alkyl, optionally substituted with up to three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(D) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(E) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(F) $-(CH_2)_{1-2}-S(O)_{0-2}(C_1-C_6\text{ alkyl})$,

(F) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(G) $-(C_1-C_4\text{ alkyl})-R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined for R_{1-aryl},

(H) $-(C_1-C_4\text{ alkyl})-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

(I) $-(C_1-C_4\text{ alkyl})-R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

- (J) $-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,
- (K) $-R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,
- (M) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C'-aryl}$ where R_{C-4} is $-O-$, $-S-$ or
 $-NR_{C-5}-$ where R_{C-5} is C_1-C_6 alkyl, and where $R_{C'-aryl}$ is defined above,
- (N) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C-heteroaryl}$ where R_{C-4} and $R_{C-heteroaryl}$
are as defined above, and
- (O) $-R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,
and where R_{C-3} is the same or different and is:
- (A) $-H$,
- (B) $-C_1-C_6$ alkyl optionally substituted with one, two or three
substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$,
 $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_6 alkoxy, $-O-$ phenyl, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as
defined above,
- (C) C_2-C_6 alkenyl with one or two double bonds, optionally
substituted with one, two or three substituents selected from the group consisting of C_1-
 C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_6 alkoxy, $-O-$ phenyl, and $-NR_{1-a}R_{1-}$
 b where R_{1-a} and R_{1-b} are as defined above,
- (D) C_2-C_6 alkynyl with one or two triple bonds, optionally
substituted with one, two or three substituents selected from the group consisting of C_1-
 C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_6 alkoxy, $-O-$ phenyl, and $-NR_{1-a}R_{1-}$
 b where R_{1-a} and R_{1-b} are as defined above,
- (E) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one,
two or three substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_6 alkoxy, $-O-$ phenyl, $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as
defined above,
- (F) $-R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,
- (G) $-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,
- (H) $-R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,
- (I) $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,
- (J) $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

or

- (K) -(C₁-C₄ alkyl)-R_{C-heterocycle} where R_{C-heterocycle} is as defined above,
- (XVI) -CH(R_{C-aryl})₂ where R_{C-aryl} are the same or different and are as defined above,
- (XVII) -CH(R_{C-heteroaryl})₂ where R_{C-heteroaryl} are the same or different and are as defined above,
- (XVIII) -CH(R_{C-aryl})(R_{C-heteroaryl}) where R_{C-aryl} and R_{C-heteroaryl} are as defined above,
- (XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle} where R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle} are as defined above where one carbon of cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with NH, NR_{N-5}, O, or S(=O)₀₋₂, and where cyclopentyl, cyclohexyl, or cycloheptyl can be optionally substituted with one or two -C₁-C₃ alkyl, -F, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, =O, or -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
- (XX) C₂-C₁₀ alkenyl containing one or two double bonds optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
- (XXI) C₂-C₁₀ alkynyl containing one or two triple bonds optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
- (XXI) -(CH₂)₀₋₁-CHR_{C-6}-(CH₂)₀₋₁-R_{C-aryl} where R_{C-aryl} is as defined above and R_{C-6} is -(CH₂)₀₋₆-OH,
- (XXII) -(CH₂)₀₋₁-CHR_{C-6}-(CH₂)₀₋₁-R_{C-heteroaryl} where R_{C-heteroaryl} and R_{C-6} is as defined above,
- (XXIII) -CH(-R_{C-aryl} or R_{C-heteroaryl})-CO-O(C₁-C₄ alkyl) where R_{C-aryl} and R_{C-heteroaryl} are as defined above,
- (XXIV) -CH(-CH₂-OH)-CH(-OH)-phenyl-NO₂,
- (XXV) (C₁-C₆ alkyl)-O-(C₁-C₆ alkyl)-OH,
- (XXVII) -CH₂-NH-CH₂-CH(-O-CH₂-CH₃)₂, or

(XXVIII) – $(CH_2)_{0-6}-C(=NR_{1-a})(NR_{1-a}R_{1-b})$ where R_{1-a} and R_{1-b} are as defined above,

where R_{C-A} is H, $C_1 - C_{10}$ alkyl, $C_2 - C_{10}$ alkenyl and alkynyl, phenyl, $C_1 - C_4$ alkyl- R_{N-aryl} , $C_1 - C_4$ alkyl- $R_{N-heteroaryl}$, $C_1 - C_4$ alkyl-C3-C7 cycloalkyl, or $C_1 - C_4$ alkyl- $R_{1-heterocycle}$, wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, -C(O)O-R_{1-a}, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H, C_1-C_6 alkyl or phenyl;

where R_{C-A} , -Z-R_C, and the nitrogen atom to which they attach may cyclize to form a ring or fused rings chosen from the group consisting of 5-8 membered heterocyclics having up to 2 heteroatoms in addition to the ring nitrogen defined above chosen from the group consisting of N, O, and S, which may optionally be fused with one, or two phenyl, pyridyl, cyclohexyl, piperidinyl or morpholinyl,

where the ring or fused rings may optionally have one, two, or three substituents independently chosen from the group of:

(1) C_1-C_6 alkyl,
 C_2-C_6 alkenyl with one or two double bonds, or
 C_2-C_6 alkynyl with one or two triple bonds, wherein each may be optionally substituted with one, two, or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

- (2) -F, Cl, -Br, or -I,
(3) $-C_1-C_6$ alkoxy optionally substituted with one, two, or three -F,
(4) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,
(5) -OH,
(6) -C≡N,
(7) =O (oxo),
(8) -CO-(C_1-C_4 alkyl),
(9) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or
(10)-CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

or a pharmaceutically acceptable salt thereof.

16. A disubstituted amine of claim 15, wherein R₁ is:

- $(CH_2)_{0-1}-(R_{1-aryl})$, or
- $(CH_2)_{n-1}-(R_{1-heteroaryl})$.

17. A disubstituted amine of claim 16, wherein R₁ is:

- $(CH_2)-(R_{1-aryl})$, or
- $(CH_2)-(R_{1-heteroaryl})$.

18. A disubstituted amine of claim 17, wherein R₁ is - $(CH_2)-(R_{1-aryl})$ where R_{1-aryl} is phenyl.

19. A disubstituted amine of claim 18, wherein R₁ is substituted with two -F.

20. A disubstituted amine of claim 19, wherein the -F substitutions are on the -3 and -5 positions.

21. A disubstituted amine of claim 15, wherein R₂ and R₃ are both -H.

22. A disubstituted amine of claim 15, wherein R_C is:

- C₁-C₈ alkyl,
- $(CH_2)_{0-3}-(C_3-C_7)$ cycloalkyl,
- $(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$,
- $(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$,
- $(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$, or
- cyclopentyl or -cyclohexyl ring fused to R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle}.

23. A disubstituted amine of claim 22, wherein R_C is:

- $(CH_2)_{0-3}-(C_3-C_7)$ cycloalkyl,
- $(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$,

~~- $(CR_{C-x}R_{C-y})_{0-4}$ - R_C -heteroaryl,
- $(CR_{C-x}R_{C-y})_{0-4}$ - R_C -heterocycle,
-cyclopentyl or -cyclohexyl ring fused to a R_C -aryl or R_C -heteroaryl or R_C -heterocycle.~~

24. A disubstituted amine of claim 23, wherein R_C is:

~~- $(CR_{C-x}R_{C-y})_{0-4}$ - R_C -aryl,
- $(CR_{C-x}R_{C-y})_{0-4}$ - R_C -heteroaryl,
-cyclopentyl or -cyclohexyl ring fused to a R_C -aryl or R_C -heteroaryl or R_C -heterocycle.~~

25. A disubstituted amine of claim 24, wherein R_C is:

~~- $(CR_{C-x}R_{C-y})_{0-4}$ - R_C -aryl where R_C -aryl is phenyl.~~

26. A disubstituted amine of claim 25, wherein said phenyl is substituted in the 3-position or 3,5-positions.

27. A disubstituted amine of claim 15, wherein R_{C-A} is:

~~-methyl, or
-ethyl.~~

28. A disubstituted amine of claim 15, wherein Z is:

~~- $C(O)$ -, or
- $C(O)-X_{N-1}$ - where X_{N-1} is selected from the group consisting of -O-, -S- and -NR'-.~~

29. A disubstituted amine of claim 15, wherein R_N is:

~~- $R_{N-1}-X_N$ - where X_N is -CO-, where R_{N-1} is R_{N-aryl} or $R_{N-heteroaryl}$ where R_{N-aryl} is phenyl where the substitution on phenyl is 1,3-, and where R_{N-aryl} or $R_{N-heteroaryl}$ are substituted with one -CO-NR_{N-2}R_{N-3},~~

~~- $R_{N-1}-X_N$ - where X_N is -CO-, where R_{N-1} is R_{N-aryl} or $R_{N-heteroaryl}$ where R_{N-aryl} is phenyl substituted with one C₁ alkyl where the substitution on the phenyl is 1,3,5-, and where R_{N-aryl} or $R_{N-heteroaryl}$ are substituted with one -CO-NR_{N-2}R_{N-3}, or~~

~~-R_{N-1}-X_{N-} where X_N is -CO-, where R_{N-1} is R_N-heteroaryl where R_N-heteroaryl is substituted with one -CO-NR_{N-2}R_{N-3}.~~

30. A disubstituted amine of claim 29, wherein R_{N-2} and R_{N-3} are the same and are C₃ alkyl.

31. A disubstituted amine of claim 29, wherein R_{N-1}-X_{N-} where X_N is -CO-, where R_{N-1} is R_N-aryl where R_N-aryl is phenyl substituted with one -CO-NR_{N-2}R_{N-3} where the substitution on phenyl is 1,3-.

32. A disubstituted amine of claim 29, wherein R_{N-1}-X_{N-} where X_N is -CO-, where R_{N-1} is R_N-aryl where R_N-aryl is phenyl substituted with one C₁ alkyl and with one -CO-NR_{N-2}R_{N-3} where the substitution on the phenyl is 1,3,5-.

33. A disubstituted amine of claim 29, wherein X_N is -CO-, or -SO₂-.

34. A disubstituted amine of claim 29, wherein X_N is -CO-.

35. A compound according to claim 11 or claim 15 selected from the group consisting of:

6-({[(2S,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]benzoyl}amino)-2-hydroxybutyl](ethyl)amino]carbonyl}amino)hexanoic acid,
N¹-((1S,2S)-1-(3,5-difluorobenzyl)-3-{ethyl[(isobutylamino)carbonyl]amino}-2-hydroxypropyl)-N³,N³-dipropylisophthalamide,
N¹-[(1S,2S)-3-[(butylsulfonyl)(ethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N³,N³-dipropylisophthalamide,
N¹-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{(2S)-2-[(isobutylamino)carbonyl]piperidinyl}propyl)-5-methyl-N³,N³-dipropylisophthalamide,
N¹-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(4-methyl-1-piperazinyl)propyl]-5-methyl-N³,N³-dipropylisophthalamide,

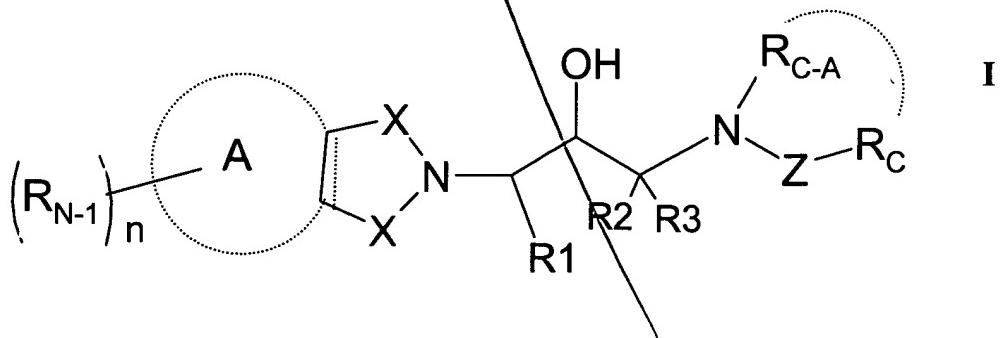
~~N¹-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-(isobutylamino)-2-oxoethyl](methyl)amino]propyl}-5-methyl-N³,N³-dipropylisophthalamide,~~

~~N¹-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-2-(isobutylamino)-1-methyl-2-oxoethyl](methyl)amino]propyl}-5-methyl-N³,N³-dipropylisophthalamide,~~

~~N¹-[(1S,2R)-1-benzyl-2-hydroxy-3-(1,3-thiazolidin-3-yl)propyl]-N³,N³-dipropylisophthalamide, and~~

~~N¹-{(1S,2R)-1-benzyl-3-[4-(4-fluorophenyl)-1-piperazinyl]-2-hydroxypropyl}-N³,N³-dipropylisophthalamide.~~

36. A method of treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment which comprises administration of a therapeutically effective amount of a compound selected from the group consisting of a disubstituted amine of formula (I)



where R₁ is:

(I) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, C₁-C₇ alkyl (optionally substituted with C₁-C₃ alkyl and C₁-C₃ alkoxy), -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl, and -OC=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(II) -CH₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(III) -CH₂-CH₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(IV) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(V) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(VI) -(CH₂)_{n1}-(R_{1-aryl}) where n₁ is zero or one and where R_{1-aryl} is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A) C₁-C₆ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(B) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(C) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(D) -F, Cl, -Br or -I,

(E) -C₁-C₆ alkoxy optionally substituted with one, two, or three -F,

(G) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,

- (H) -OH,
(I) -C≡N,
(J) C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
(K) -CO-(C₁-C₄ alkyl),
(L) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
(M) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or
(N) -SO₂-(C₁-C₄ alkyl),
(VII) -(CH₂)_{n1}-(R_{1-heteroaryl}) where n₁ is as defined above and where R_{1-heteroaryl} is selected from the group consisting of:

pyridinyl,
pyrimidinyl,
quinolinyl,
benzothienyl,
indolyl,
indolinyl,
pyridazinyl,
pyrazinyl,
isoquinolyl,
quinazolinyl,
quinoxalinyl,
phthalazinyl,
imidazolyl,
isoxazolyl,
pyrazolyl,
oxazolyl,
thiazolyl,
indolizinyl,
indazolyl,
benzothiazolyl,

benzimidazolyl,
benzofuranyl,
furanyl,
thienyl,
pyrrolyl,
oxadiazolyl,
thiadiazolyl,
triazolyl,
tetrazolyl,
oxazolopyridinyl,
imidazopyridinyl,
isothiazolyl,
naphthyridinyl,
cinnolinyl,
carbazolyl,
beta-carbolinyl,
isochromanyl,
chromanyl,
tetrahydroisoquinolinyL
isoindolinyl,
isobenzotetrahydrofuranyl,
isobenzotetrahydrothienyl,
isobenzothienyl,
benzoxazolyl,
pyridopyridinyl,
benzotetrahydrofuranyl,
benzotetrahydrothienyl,
purinyl,
benzodioxolyl,
triazinyl,
phenoxyazinyl,

phenothiazinyl,
pteridinyl,
benzothiazolyl,
imidazopyridinyl,
imidazothiazolyl,
dihydrobenzisoxazinyl,
benzisoxazinyl,
benzoxazinyl,
dihydrobenzisothiazinyl,
benzopyranyl,
benzothiopyranyl,
coumarinyl,
isocoumarinyl,
chromonyl,
chromanonyl,
pyridinyl-N-oxide,
tetrahydroquinolinyl
~~dihydroquinolinyl~~
dihydroquinolinonyl
dihydroisoquinolinonyl
dihydrocoumarinyl
dihydroisocoumarinyl
isoindolinonyl
benzodioxanyl
benzoxazolinonyl
pyrrolyl N-oxide,
pyrimidinyl N-oxide,
pyridazinyl N-oxide,
pyrazinyl N-oxide,
quinolinyl N-oxide,
indolyl N-oxide,

indolinyl N-oxide,
isoquinolyl N-oxide,
quinazolinyl N-oxide,
quinoxaliny N-oxide,
phthalazinyl N-oxide,
imidazolyl N-oxide,
isoxazolyl N-oxide,
oxazolyl N-oxide,
thiazolyl N-oxide,
indolizinyl N-oxide,
indazolyl N-oxide,
benzothiazolyl N-oxide,
benzimidazolyl N-oxide,
pyrrolyl N-oxide,
oxadiazolyl N-oxide,
thiadiazolyl N-oxide,
triazolyl N-oxide,
tetrazolyl N-oxide,
benzothiopyranyl S-oxide, and
benzothiopyranyl S,S-dioxide,

where the $R_{1\text{-heteraryl}}$ group is bonded to $-(CH_2)_{n1}-$ by any ring atom of the parent R_N -heteraryl group substituted by hydrogen such that the new bond to the $R_{1\text{-heteraryl}}$ group replaces the hydrogen atom and its bond, where heteraryl is optionally substituted with one, two, three, or four:

(1) $C_1\text{-}C_6$ alkyl optionally substituted with one, two or three substituents selected from the group consisting of $C_1\text{-}C_3$ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(2) $C_2\text{-}C_6$ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,

(3) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(4) -F, Cl, -BR, or -I,

(6) -C₁-C₆ alkoxy optionally substituted with one, two, or three -F,

(7) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,

(8) -OH,

(9) -C≡N,

(10) C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(11) -CO-(C₁-C₄ alkyl),

(12) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(13) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or

(14) -SO₂-(C₁-C₄ alkyl), with the proviso that when n₁ is zero R_{1-heteraryl} is not bonded to the carbon chain by nitrogen, or

(VIII) -(CH₂)_{n1}-(R_{1-heterocycle}) where n₁ is as defined above and R_{1-heterocycle} is selected from the group consisting of:

morpholinyl,

thiomorpholinyl,

thiomorpholinyl S-oxide,

thiomorpholinyl S,S-dioxide,

piperazinyl,

homopiperazinyl,

pyrrolidinyl,

pyrrolinyl,

tetrahydropyranyl,

piperidinyl,

tetrahydrofuranyl,

tetrahydrothienyl,

homopiperidinyl,
homomorpholinyl,
homothiomorpholinyl,
homothiomorpholinyl S,S-dioxide,
oxazolidinonyl,
dihydropyrazolyl,
dihydropyrrolyl,
dihydropyrazinyl,
dihydropyridinyl,
dihydropyrimidinyl,
dihydrofuryl,
dihydopyranyl,
tetrahydrothienyl S-oxide,
tetrahydrothienyl S,S-dioxide, and
homothiomorpholinyl S-oxide,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heterocycle}}$ group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three, or four:

(1) $C_1\text{-}C_6$ alkyl optionally substituted with one, two or three substituents selected from the group consisting of $C_1\text{-}C_3$ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(2) $C_2\text{-}C_6$ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,

(3) $C_2\text{-}C_6$ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,

(4) -F, Cl, -Br, or -I,

- (5) C₁-C₆ alkoxy,
 (6) -C₁-C₆ alkoxy substituted with one, two, or three -F,
 (7) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,
 (8) -OH,
 (9) -C≡N,
 (10) C₃-C₇ cycloalkyl, optionally substituted with one, two
 or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃,
 C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
 (11) -CO-(C₁-C₄ alkyl),
 (12) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined
 above,
 (13) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined
 above,
 (14) -SO₂-(C₁-C₄ alkyl), or
 (15) =O, with the proviso that when n₁ is zero R₁-heterocycle is
 not bonded to the carbon chain by nitrogen;

where R₂ is:

- (I)-H,
 (II) C₁-C₆ alkyl, optionally substituted with one, two or three substituents
 selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH,
 -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
 (III) -(CH₂)₀₋₄-R₂₋₁ where R₂₋₁ is R₁-aryl or R₁-heteroaryl where R₁-aryl and R₁-
 heteroaryl are as defined above;
 (IV) C₂-C₆ alkenyl with one or two double bonds, optionally substituted
 with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -
 SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
 (V) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with
 one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -
 C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl, or

(VI) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

where R₃ is:

(I) -H,

(II) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(III) $-(CH_2)_{0-4}-R_{2-1}$ where R₂₋₁ is R_{1-aryl} or R_{1-heteroaryl} where R_{1-aryl} and R_{1-heteroaryl} are as defined above;

(IV) C₂-C₆ alkenyl with one or two double bonds,

(V) C₂-C₆ alkynyl with one or two triple bonds, or

(VI) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl, where R₂ and R₃ are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO₂-, and -NR_{N-2-},

where R_{N-2} is selected from the group consisting of:

(a) -H,

(b) -C₁-C₆ alkyl optionally substituted with one

substituent selected from the group consisting of:

(i) -OH, and

(ii) -NH₂,

(c) -C₁-C₆ alkyl optionally substituted with one to

three -F, -Cl, -Br, or -I,

(d) -C₃-C₇ cycloalkyl,

(e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),

(f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),

- triple bond,
- (g) $-C_2-C_6$ alkenyl with one or two double bonds,
 - (h) $-C_2-C_6$ alkynyl with one or two triple bonds,
 - (i) $-C_1-C_6$ alkyl chain with one double bond and one
 - (j) $-R_{1-aryl}$ where R_{1-aryl} is as defined above, and
 - (k) $-R_{1-heteroaryl}$ where $R_{1-heteroaryl}$ is as defined above;

where X is independently chosen from the group consisting of:

- $-C(O)-$,
- $-CH_2-$,
- $-CH_2-CH_2-$, and
- $-CH_2-C(O)-$;

wherein in the rings drawn, a dotted line indicates an optional double bond or an optional ring;

wherein ring A is phenyl, cyclohexyl, cyclopentyl, pyridyl, pyrimidinyl, pyrazinyl or is absent; and

where R_{N-1} is selected from the group consisting of:

- (1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

- (2) $-OH$,
- (3) $-NO_2$,
- (4) $-F$, $-Cl$, $-Br$, or $-I$,
- (5) $-CO-OH$,
- (6) $-C\equiv N$,
- (7) $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are selected from the group consisting of:

- (a) $-H$,
- (b) $-C_1-C_6$ alkyl optionally substituted with one substituent selected from the group consisting of:

- (i) -OH, and
 (ii) -NH₂,
 (c) -C₁-C₆ alkyl optionally substituted with one to
 three -F, -Cl, -Br, or -I,
 triple bond,
- (d) -C₃-C₇ cycloalkyl,
 (e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),
 (f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),
 (g) -C₂-C₆ alkenyl with one or two double bonds,
 (h) -C₂-C₆ alkynyl with one or two triple bonds,
 (i) -C₁-C₆ alkyl chain with one double bond and one
 triple bond,
 double bonds),
 triple bonds),
 above,
- (j) -R₁-aryl where R₁-aryl is as defined above, and
 (k) -R₁-heteroaryl where R₁-heteroaryl is as defined above,
 (8) -(CH₂)₀₋₄-CO-(C₁-C₁₂ alkyl),
 (9) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkenyl with one, two, or three
 double bonds),
 (10) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkynyl with one, two, or three
 triple bonds),
 (11) -(CH₂)₀₋₄-CO-(C₃-C₇ cycloalkyl),
 (12) -(CH₂)₀₋₄-CO-R₁-aryl where R₁-aryl is as defined above,
 (13) -(CH₂)₀₋₄-CO-R₁-heteroaryl where R₁-heteroaryl is as defined
 above,
 (14) -(CH₂)₀₋₄-CO-R₁-heterocycle where R₁-heterocycle is as
 defined above,
 (15) -(CH₂)₀₋₄-CO-R_{N-4} where R_{N-4} is selected from the
 group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl,
 homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide,
 homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is
 optionally substituted with one, two, three, or four of: C₁-C₆ alkyl,
 (16) -(CH₂)₀₋₄-CO-O-R_{N-5} where R_{N-5} is selected from the
 group consisting of:

- (a) C₁-C₆ alkyl,
- (b) -(CH₂)₀₋₂-(R_{1-aryl}) where R_{1-aryl} is as defined above,
- (c) C₂-C₆ alkenyl containing one, or two double bonds,
- (d) C₂-C₆ alkynyl containing one, or two triple bonds,
- (e) C₃-C₇ cycloalkyl, and
- (f) -(CH₂)₀₋₂-(R_{1-heteroaryl}) where R_{1-heteroaryl} is as defined above,
- (17) -(CH₂)₀₋₄-SO₂-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined above,
- (18) -(CH₂)₀₋₄-SO-(C₁-C₈ alkyl),
- (19) -(CH₂)₀₋₄-SO₂-(C₁-C₁₂ alkyl),
- (20) -(CH₂)₀₋₄-SO₂-(C₃-C₇ cycloalkyl),
- (21) -(CH₂)₀₋₄-N(H or R_{N-5})-CO-O-R_{N-5} where R_{N-5} can be the same or different and is as defined above,
- (22) -(CH₂)₀₋₄-N(H or R_{N-5})-CO-N(R_{N-5})₂, where R_{N-5} can be the same or different and is as defined above,
- (23) -(CH₂)₀₋₄-N-CS-N(R_{N-5})₂, where R_{N-5} can be the same or different and is as defined above,
- (24) -(CH₂)₀₋₄-N(-H or R_{N-5})-CO-R_{N-2} where R_{N-5} and R_{N-2} can be the same or different and are as defined above,
- (25) -(CH₂)₀₋₄-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} can be the same or different and are as defined above,
- (26) -(CH₂)₀₋₄-R_{N-4} where R_{N-4} is as defined above,
- (27) -(CH₂)₀₋₄-O-CO-(C₁-C₆ alkyl),
- (28) -(CH₂)₀₋₄-O-P(O)-(OR_{N-aryl-1})₂ where R_{N-aryl-1} is -H or C₁-C₄ alkyl,
- (29) -(CH₂)₀₋₄-O-CO-N(R_{N-5})₂ where R_{N-5} is as defined above,

- (30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$ where R_{N-5} is as defined above,
- (31) $-(CH_2)_{0-4}-O-(R_{N-5})_2$ where R_{N-5} is as defined above,
- (32) $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$ where R_{N-5} is as defined above,
- (33) $-(CH_2)_{0-4}-S-(R_{N-5})_2$ where R_{N-5} is as defined above,
- (34) $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl}$ optionally substituted with one, two, three, four, or five of: $-F$),
- (35) C_3-C_7 cycloalkyl,
- (36) C_2-C_6 alkenyl with one or two double bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,
- (37) C_2-C_6 alkynyl with one or two triple bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,
- (38) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as described above, and
- (39) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl;
- where n is equal to 0, 1, 2 or 3;
- where Z is selected from the group consisting of:
- (A) $-C(O)-$,
 - (B) $-S(O)_{1-2}-$,
 - (C) $-C(O)-X_{N-1}-$ where X_{N-1} is selected from the group consisting of $-O-$, $-S-$ and $-NR'$ and where R' is as defined above; and
 - (D) a single bond;

where R_C is:

- (I) C_1-C_{10} alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$,

-SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O-phenyl, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -OC=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -S(=O)₀₋₂ R_{1-a} where R_{1-a} is as defined above, -NR_{1-a}C=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -C=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, and -S(=O)₂ NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(II) -(CH₂)₀₋₃-(C₃-C₈) cycloalkyl where cycloalkyl can be optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O-phenyl, -CO-OH, -CO-O-(C₁-C₄ alkyl), and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(III) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl} where R_{C-x} and R_{C-y} are

(I) -H,

(J) C₁-C₄ alkyl optionally substituted with one or two -OH,,

(K) C₁-C₄ alkoxy optionally substituted with one, two, or three -F,

(L) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl,

(M) C₂-C₆ alkenyl containing one or two double bonds,

(N) C₂-C₆ alkynyl contianing one or two triple bonds,

(O) phenyl-,

(P) C₀-C₄ alkyl-C(O) NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

and where R_{C-x} and R_{C-y} are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO₂-, -NR_{N-2-} and R_{C-aryl} is the same as R_{N-aryl} and where R_{C-aryl} may optionally be substituted with -C₀-C₄ alkyl-C(O) NR_{1-a}R_{1-b}, C₀-C₄ alkylC(O) OR_{1-a} where R_{1-a} and R_{1-b} are as defined above,

(IV) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-heteroaryl} where R_{C-heteroaryl} is the same as R_{N-heteroaryl} and R_{C-x} and R_{C-y} are as defined above,

(V) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl}-R_{C-aryl} where R_{C-aryl}, R_{C-x} and R_{C-y} are as defined above,

(VI) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-aryl}-R_{C-heteroaryl}$ where R_{C-aryl} , $R_{C-heteroaryl}$, R_{C-x} and R_{C-y} are as defined above,

(VII) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-heteroaryl}-R_{C-aryl}$ where $R_{C-heteroaryl}$, R_{C-aryl} , R_{C-x} and R_{C-y} are as defined above,

(VIII) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-heteroaryl}-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$, R_{C-x} and R_{C-y} are as defined above,

(IX) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-aryl}-R_{C-heterocycle}$ where $R_{C-heterocycle}$ is the same as $R_{1-heterocycle}$, and R_{C-aryl} , R_{C-x} and R_{C-y} are as defined above,

(X) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-heteroaryl}-R_{C-heterocycle}$ where $R_{C-heteroaryl}$, $R_{C-heterocycle}$, R_{C-x} and R_{C-y} are as defined above,

(XI) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-heterocycle}-R_{C-aryl}$ where $R_{C-heterocycle}$, R_{C-aryl} , R_{C-x} and R_{C-y} are as defined above,

(XII) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-heterocycle}-R_{C-heteroaryl}$ where $R_{C-heterocycle}$, $R_{C-heteroaryl}$, R_{C-x} and R_{C-y} are as defined above,

(XIII) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-heterocycle}-R_{C-heterocycle}$ where $R_{C-heterocycle}$, R_{C-x} and R_{C-y} are as defined above,

(XIV) $-(CR_{C-x}RC_{-y})_{0-4}-R_{C-heterocycle}$ where $R_{C-heterocycle}$, R_{C-x} , and R_{C-y} are as defined above,

(XV) $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$ where R_{C-3} is as defined below and R_{C-1} , R_{C-2} are the same or different and are selected from the group consisting of:

(A) -H,

(B) $-C_1-C_6$ alkyl, optionally substituted with one, two, or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(D) C_2-C_6 alkenyl with one, or two double bonds, optionally substituted with one, two, or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(E) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two, or three substituents selected from the group consisting of C_1-C_3

C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(F) -(CH₂)₁₋₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(F) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl, optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(G) -(C₁-C₄ alkyl)-R_{C'-aryl} where R_{C'-aryl} is as defined for R_{1-aryl},

(H) -(C₁-C₄ alkyl)-R_{C-heteroaryl} where R_{C-heteroaryl} is as defined above,

(I) -(C₁-C₄ alkyl)-R_{C-heterocycle} where R_{C-heterocycle} is as defined above,

(J) -R_{C-heteroaryl} where R_{C-heteroaryl} is as defined above,

(K) -R_{C-heterocycle} where R_{C-heterocycle} is as defined above,

(M) -(CH₂)₁₋₄-R_{C-4}-(CH₂)₀₋₄-R_{C'-aryl} where R_{C-4} is -O-, -S- or -NR_{C-5-} where R_{C-5} is C₁-C₆ alkyl, and where R_{C'-aryl} is defined above,

(N) -(CH₂)₁₋₄-R_{C-4}-(CH₂)₀₋₄-R_{C-heteroaryl} where R_{C-4} and R_{C-heteroaryl} are as defined above, and

(O) -R_{C'-aryl} where R_{C'-aryl} is as defined above,

and where R_{C-3} is the same or different and is:

(a) -H,

(b) -C₁-C₆ alkyl optionally substituted with one, two or

three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(c) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(d) C₂-C₆ alkynyl with one, or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of C₁-

C_3 -alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(e) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(f) -R_{C'-aryl} where R_{C'-aryl} is as defined above,

(g) -R_{C-heteroaryl} where R_{C-heteroaryl} is as defined above,

(h) -R_{C-heterocycle} where R_{C-heterocycle} is as defined above,

(i) -(C₁-C₄ alkyl)-R_{C'-aryl} where R_{C'-aryl} is as defined above,

(j) -(C₁-C₄ alkyl)-R_{C-heteroaryl} where R_{C-heteroaryl} is as defined above,

(k) -(C₁-C₄ alkyl)-R_{C-heterocycle} where R_{C-heterocycle} is as defined above,

(XVI) -CH(R_{C-aryl})₂ where R_{C-aryl} are the same or different and are as defined above,

(XVII) -CH(R_{C-heteroaryl})₂ where R_{C-heteroaryl} are the same or different and are as defined above,

(XVIII) -CH(R_{C-aryl})(R_{C-heteroaryl}) where R_{C-aryl} and R_{C-heteroaryl} are as defined above,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle} where R_{C-aryl} or R_{C-heteroaryl} or R_{C-heterocycle} are as defined above where one carbon of cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with NH, NR_{N-5}, O, or S(=O)₀₋₂, and where cyclopentyl, cyclohexyl, or cycloheptyl can be optionally substituted with one, or two -C₁-C₃ alkyl, -F, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, =O, or -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(XX) C₂-C₁₀ alkenyl containing one or two double bonds optionally substituted with one, two, or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₆ alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(XXI) C_2-C_{10} alkynyl containing one, or two triple bonds optionally substituted with one, two, or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(XXI) $-(CH_2)_{0-1}-CHR_{C-6}-(CH_2)_{0-1}-R_{C-aryl}$ where R_{C-aryl} is as defined above and R_{C-6} is $-(CH_2)_{0-6}-OH$,

(XXII) $-(CH_2)_{0-1}-CHR_{C-6}-(CH_2)_{0-1}-R_{C-heteroaryl}$ where R_{C-heteroaryl} and R_{C-6} is as defined above,

(XXIII) $-CH(-R_{C-aryl} \text{ or } R_{C-heteroaryl})-CO-O(C_1-C_4 \text{ alkyl})$ where R_{C-aryl} and R_{C-heteroaryl} are as defined above,

(XXIV) $-CH(-CH_2-OH)-CH(-OH)-phenyl-NO_2$,

(XXV) $(C_1-C_6 \text{ alkyl})-O-(C_1-C_6 \text{ alkyl})-OH$,

(XXVII) $-CH_2-NH-CH_2-CH(-O-CH_2-CH_3)_2$, or

(XXVIII) $-(CH_2)_{0-6}-C(=NR_{1-a})(NR_{1-a}R_{1-b})$ where R_{1-a} and R_{1-b} are as defined above,

where R_{C-A} is H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl and alkynyl, phenyl, C_1-C_4 alkyl-R_{N-aryl}, C_1-C_4 alkyl-R_{N-heteroaryl}, C_1-C_4 alkyl-C₃-C₇ cycloalkyl, or C_1-C_4 alkyl-R_{1-heterocycle}, wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, -C(O)O-R_{1-a}, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H, C_1-C_6 alkyl or phenyl;

where R_{C-A}, -Z-R_C, and the nitrogen atom to which they attach may cyclize to form a ring or fused rings chosen from the group consisting of 5-8 membered heterocyclics having up to 2 heteroatoms in addition to the ring nitrogen defined above chosen from the group consisting of N, O, and S, which may optionally be fused with one, or two phenyl, pyridyl, cyclohexyl, piperidinyl or morpholinyl,

where the ring or fused rings may optionally have one, two, or three substituents independently chosen from the group of:

(1) C_1-C_6 alkyl,

C_2-C_6 alkenyl with one or two double bonds, or

C_2-C_6 alkynyl with one or two triple bonds, wherein each may be optionally substituted with one, two, or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

- (3) -F, Cl, -Br, or -I,
- (10) -C₁-C₆ alkoxy optionally substituted with one, two, or three -F,
- (11) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,
- (12) -OH,
- (13) -C≡N,
- (14) =O (oxo),
- (15) -CO-(C₁-C₄ alkyl),
- (16) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or
- (10)-CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above;

or a pharmaceutically acceptable salt thereof.

37. A method of treatment according to claim 36, wherein the disease is Alzheimer's disease.

38. A method of treatment according to claim 36, wherein the method is helping prevent or delay the onset of Alzheimer's disease.

39. A method of treatment according to claim 36, wherein the disease is mild cognitive impairment.

40. A method of treatment according to claim 36, wherein the disease is Down's syndrome.

41. A method of treatment according to claim 36, wherein the disease is Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type.

42. A method of treatment according to claim 36, wherein the disease is cerebral amyloid angiopathy.
43. A method of treatment according to claim 36, wherein the disease is degenerative dementias.
44. A method of treatment according to claim 36, wherein the disease is diffuse Lewy body type of Alzheimer's disease.
45. A method of treatment according to claim 36, wherein the method is treating an existing disease.
46. A method of treatment according to claim 36, wherein the method is preventing a disease from developing.
47. A method of treatment according to claim 36, wherein the therapeutically effective amount for oral administration is from about 0.1 mg/day to about 1,000 mg/day; for parenteral, sublingual, intranasal, intrathecal administration is from about 0.5 to about 100 mg/day; for depo administration and implants is from about 0.5 mg/day to about 50 mg/day; for topical administration is from about 0.5 mg/day to about 200 mg/day; for rectal administration is from about 0.5 mg to about 500 mg.
48. A method of treatment according to claim 47, wherein the therapeutically effective amount for oral administration is from about 1 mg/day to about 100 mg/day and for parenteral administration is from about 5 to about 50 mg daily.
49. A method of treatment according to claim 48 where the therapeutically effective amount for oral administration is from about 5 mg/day to about 50 mg/day.
50. A method of treatment according to claim 36, wherein R₁ is:
-(CH₂)₀₋₁-(R₁-aryl), or

$\backslash(CH_2)_{n1}-(R_1\text{-heteroaryl})$.

51. A method of treatment according to claim 50, wherein R_1 is:

$-(CH_2)-(R_1\text{-aryl})$, or

$-(CH_2)-(R_1\text{-heteroaryl})$.

52. A method of treatment according to claim 51, wherein R_1 is $-(CH_2)-(R_1\text{-aryl})$ where $R_1\text{-aryl}$ is phenyl.

53. A method of treatment according to claim 52, wherein R_1 is substituted with two -F.

54. A method of treatment according to claim 53, wherein the -F substitutions are on the -3 and -5 positions.

55. A method of treatment according to claim 36, wherein R_2 and R_3 are both -H.

56. A method of treatment according to claim 36, wherein R_C is:

$-C_1-C_8$ alkyl,

$-(CH_2)_{0-3}-(C_3-C_7)$ cycloalkyl,

$-(CR_{C-x}RC-y)_{0-4}-R_C\text{-aryl}$,

$-(CR_{C-x}RC-y)_{0-4}-R_C\text{-heteroaryl}$,

$-(CR_{C-x}RC-y)_{0-4}-R_C\text{-heterocycle}$, or

-cyclopentyl or -cyclohexyl ring fused to $R_C\text{-aryl}$ or $R_C\text{-heteroaryl}$ or $R_C\text{-heterocycle}$.

57. A method of treatment according to claim 56, wherein R_C is:

$-(CH_2)_{0-3}-(C_3-C_7)$ cycloalkyl,

$-(CR_{C-x}RC-y)_{0-4}-R_C\text{-aryl}$,

$-(CR_{C-x}RC-y)_{0-4}-R_C\text{-heteroaryl}$,

$-(CR_{C-x}RC-y)_{0-4}-R_C\text{-heterocycle}$, or

-cyclopentyl or -cyclohexyl ring fused to a $R_C\text{-aryl}$ or $R_C\text{-heteroaryl}$ or $R_C\text{-heterocycle}$.

58. A method of treatment according to claim 57, wherein R_C is:

- (CR_{C-x}R_{C-y})₀₋₄-R_C-aryl,
- (CR_{C-x}R_{C-y})₀₋₄-R_C-heteroaryl,
- cyclopentyl or -cyclohexyl ring fused to a R_C-aryl or R_C-heteroaryl or R_C-heterocycle.

59. A method of treatment according to claim 58, wherein R_C is:

- (CR_{C-x}R_{C-y})₀₋₄-R_C-aryl where R_C-aryl is phenyl.

60. A method of treatment according to claim 59, wherein said phenyl is substituted in the 3-position or 3,5-positions.

61. A method of treatment according to claim 36, wherein R_{C-A} is:

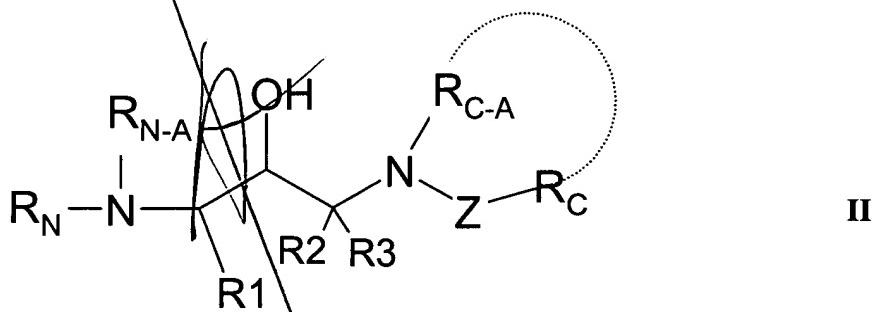
- methyl, or
- ethyl.

62. A method of treatment according to claim 36, wherein Z is:

- C(O)-, or
- C(O)-X_{N-1}- where X_{N-1} is selected from the group consisting of -O-, -S- and -NR'-.

63. A method of treatment according to claim 36 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids: acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate, camsylic, carbonic, chlorobenzoic, citric, edetic, edisyllic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycolylarsanilic, hexamic, hexylresorcinic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

64. A method of treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment which comprises administration of a therapeutically effective amount of a compound selected from the group consisting of a disubstituted amine of formula II



where R₁ is:

(I) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, C₁-C₇ alkyl (optionally substituted with C₁-C₃ alkyl and C₁-C₃ alkoxy), -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl, and -OC=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(II) -CH₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(III) -CH₂-CH₂-S(O)₀₋₂-(C₁-C₆ alkyl),

(IV) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(V) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(VI) -(CH₂)_{n1}-(R_{1-aryl}) where n₁ is zero or one and where R_{1-aryl} is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A) C_1-C_6 alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(B) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(C) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(D) -F, Cl, -Br or -I,

(E) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,

(F) -OH,

(G) -C≡N,

(H) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(I) -CO-(C_1-C_4 alkyl),

(J) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(K) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or

(N) $\text{SO}_2\text{-}(\text{C}_1\text{-}\text{C}_4 \text{ alkyl})$,
(VII) $-(\text{CH}_2)_{n_1}\text{-}(\text{R}_1\text{-heteroaryl})$ where n_1 is as defined above and where R_1 heteroaryl is selected from the group consisting of:

pyridinyl,
pyrimidinyl,
quinolinyl,
benzothienyl,
indolyl,
indolinyl,
pyridazinyl,
pyrazinyl,
isoquinolyl,
quinazolinyl,
quinoxalinyl,
phthalazinyl,
imidazolyl,
isoxazolyl,
pyrazolyl,
oxazolyl,
thiazolyl,
indolizinyl,
indazolyl,
benzothiazolyl,
benzimidazolyl,
benzofuranyl,
furanyl,
thienyl,
pyrrolyl,
oxadiazolyl,
thiadiazolyl,
triazolyl,

tetrazolyl,
oxazolopyridinyl,
imidazopyridinyl,
isothiazolyl,
naphthyridinyl,
cinnolinyl,
carbazolyl,
beta-carbolinyl,
isochromanyl,
chromanyl,
tetrahydroisoquinolinyl,
isoindolinyl,
isobenzotetrahydrofuranyl,
isobenzotetrahydrothienyl,
isobenzothienyl,
benzoxazolyl,
pyridopyridinyl,
benzotetrahydrofuranyl,
benzotetrahydrothienyl,
purinyl,
benzdioxolyl,
triazinyl,
phenoxyazinyl,
phenothiazinyl,
pteridinyl,
benzothiazolyl,
imidazopyridinyl,
imidazothiazolyl,
dihydrobenzisoxazinyl,
benzisoxazinyl,
benzoxazinyl,

dihydrobenzisothiaziny
benzopyranyl,
benzothiopyranyl,
coumarinyl,
isocoumarinyl,
chromonyl,
chromanonyl,
pyridinyl-N-oxide,
tetrahydroquinolinyl
dihydroquinolinyl
dihydroquinolinonyl
dihydroisoquinolinonyl
dihydrocoumarinyl
dihydroisocoumarinyl
isoindolinonyl
benzodioxanyl
benzoxazolinonyl
pyrrolyl N-oxide,
pyrimidinyl N-oxide,
pyridazinyl N-oxide,
pyrazinyl N-oxide,
quinolinyl N-oxide,
indolyl N-oxide,
indolinyl N-oxide,
isoquinolyl N-oxide,
quinazolinyl N-oxide,
quinoxalinyl N-oxide,
phthalazinyl N-oxide,
imidazolyl N-oxide,
isoxazolyl N-oxide,
oxazolyl N-oxide,

thiazolyl N-oxide,
indolizinyl N-oxide,
indazolyl N-oxide,
benzothiazolyl N-oxide,
benzimidazolyl N-oxide,
pyrrolyl N-oxide,
oxadiazolyl N-oxide,
thiadiazolyl N-oxide,
triazolyl N-oxide,
tetrazolyl N-oxide,
benzothiopyranyl S-oxide, and
benzothiopyranyl S,S-dioxide,

where the R_{1-heteraryl} group is bonded to -(CH₂)_{n1}- by any ring atom of the parent R_N-heteraryl group substituted by hydrogen such that the new bond to the R_{1-heteraryl} group replaces the hydrogen atom and its bond, where heteraryl is optionally substituted with one, two, three, or four:

- (1) C₁-C₆ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
- (2) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
- (3) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,
- (4) -F, Cl, -BR, or -I,
- (6) -C₁-C₆ alkoxy optionally substituted with one, two, or three -F,
- (7) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,
- (8) -OH,

(9) -C≡N,

(10) C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(11) -CO-(C₁-C₄ alkyl),

(12) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(13) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or

(14) -SO₂-(C₁-C₄ alkyl), with the proviso that when n₁ is zero R₁-heteroaryl is not bonded to the carbon chain by nitrogen, or

(VIII) -(CH₂)_{n1}-(R₁-heterocycle) where n₁ is as defined above and R₁-heterocycle is selected from the group consisting of:

morpholinyl,

thiomorpholinyl,

thiomorpholinyl S-oxide,

thiomorpholinyl S,S-dioxide,

piperazinyl,

homopiperazinyl,

pyrrolidinyl,

pyrrolinyl,

tetrahydropyranyl,

piperidinyl,

tetrahydrofuranyl,

tetrahydrothienyl,

homopiperidinyl,

homomorpholinyl,

homothiomorpholinyl,

homothiomorpholinyl S,S-dioxide,

oxazolidinonyl,

dihydropyrazolyl,

dihydropyrrolyl,

dihydropyrazinyl,

dihydropyridinyl,
dihydropyrimidinyl,
dihydrofuryl,
dihydropyranyl,
tetrahydrothienyl S-oxide,
tetrahydrothienyl S,S-dioxide, and
homothiomorpholinyl S-oxide,

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heterocycle}}$ group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three, or four:

(1) $C_1\text{-}C_6$ alkyl optionally substituted with one, two or three substituents selected from the group consisting of $C_1\text{-}C_3$ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(2) $C_2\text{-}C_6$ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,

(3) $C_2\text{-}C_6$ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,

(4) -F, Cl, -Br, or -I,

(5) $C_1\text{-}C_6$ alkoxy,

(6) - $C_1\text{-}C_6$ alkoxy substituted with one, two, or three -F,

(7) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,

(8) -OH,

(9) -C≡N,

(10) $C_3\text{-}C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1\text{-}C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1\text{-}C_6$ alkyl,

- (11) -CO-(C₁-C₄ alkyl),
 (12) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
 (13) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,
 (14) -SO₂-(C₁-C₄ alkyl), or
 (15) =O, with the proviso that when n₁ is zero R₁-heterocycle is not bonded to the carbon chain by nitrogen;

where R₂ is:

(I)-H,

(II) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(III) -(CH₂)₀₋₄-R₂₋₁ where R₂₋₁ is R₁-aryl or R₁-heteroaryl where R₁-aryl and R₁-heteroaryl are as defined above;

(IV) C₂-C₆ alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

(V) C₂-C₆ alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl, or

(VI) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

where R₃ is selected from the group consisting of:

(I)-H,

(II) C₁-C₆ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C₁-C₃ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(II) $-(CH_2)_{0-4}-R_{2-1}$ where R_{2-1} is R_{1-aryl} or $R_{1-heteroaryl}$ where R_{1-aryl} and $R_{1-heteroaryl}$ are as defined above;

(IV) C_2-C_6 alkenyl with one or two double bonds,

(V) C_2-C_6 alkynyl with one or two triple bonds, or

(VI) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or C₁-C₆ alkyl,

and where R₂ and R₃ are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO₂-, and -NR_{N-2-},

where R_{N-2} is selected from the group consisting of:

(a) -H,

(b) -C₁-C₆ alkyl optionally substituted with one

substituent selected from the group consisting of:

(i) -OH, and

(ii) -NH₂,

(c) -C₁-C₆ alkyl optionally substituted with one to

three -F, -Cl, -Br, or -I,

(d) -C₃-C₇ cycloalkyl,

(e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),

(f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),

(g) -C₂-C₆ alkenyl with one or two double bonds,

(h) -C₂-C₆ alkynyl with one or two triple bonds,

(i) -C₁-C₆ alkyl chain with one double bond and one

triple bond,

(j) -R_{1-aryl} where R_{1-aryl} is as defined above, and

(k) -R_{1-heteroaryl} where R_{1-heteroaryl} is as defined above;

where R_N is:

(I) $R_{N-1}-X_N-$ where X_N- is selected from the group consisting of:

(A) $-CO-$,

(B) $-SO_2-$,

(C) $-(CR'R'')_{1-6}$ where R' and R'' are the same or different and are
 $-H$ or C_1-C_4 alkyl,

(D) $-CO-(CR'R'')_{1-6}-X_{N-1}$ where X_{N-1} is selected from the group
 consisting of $-O-$, $-S-$ and $-NR'-$ and where R' and R'' are as defined above, and

(E) a single bond;

where R_{N-1} is selected from the group consisting of:

(A) R_{N-aryl} where R_{N-aryl} is phenyl, 1-naphthyl, 2-naphthyl,
 tetralinyl, indanyl, or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl, or dihydronaphthyl
 optionally substituted with one, two or three of the following substituents which can be
 the same or different and are:

(1) C_1-C_6 alkyl, optionally substituted with one, two or
 three substituents selected from the group consisting of C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$,
 $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined
 above,

(2) $-OH$,

(3) $-NO_2$,

(4) $-F$, $-Cl$, $-Br$, or $-I$,

(5) $-CO-OH$,

(6) $-C\equiv N$,

(7) $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the
 same or different and are selected from the group consisting of:

(a) $-H$,

(b) $-C_1-C_6$ alkyl optionally substituted with one

substituent selected from the group consisting of:

(i) $-OH$, and

(ii) $-NH_2$,

- (c) -C₁-C₆ alkyl optionally substituted with one to
three -F, -Cl, -Br, or -I,

(d) -C₃-C₇ cycloalkyl,
(e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),
(f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),
(g) -C₂-C₆ alkenyl with one or two double bonds,
(h) -C₂-C₆ alkynyl with one or two triple bonds,
(i) -C₁-C₆ alkyl chain with one double bond and one
triple bond,

(j) -R_{1-aryl} where R_{1-aryl} is as defined above, and
(k) -R_{1-heteroaryl} where R_{1-heteroaryl} is as defined above,
(8) -(CH₂)₀₋₄-CO-(C₁-C₁₂ alkyl),
(9) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkenyl with one, two or three
double bonds),

(10) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkynyl with one, two or three
triple bonds),

(11) -(CH₂)₀₋₄-CO-(C₃-C₇ cycloalkyl),
(12) -(CH₂)₀₋₄-CO-R_{1-aryl} where R_{1-aryl} is as defined above,
(13) -(CH₂)₀₋₄-CO-R_{1-heteroaryl} where R_{1-heteroaryl} is as defined
above,

(14) -(CH₂)₀₋₄-CO-R_{1-heterocycle} where R_{1-heterocycle} is as
defined above,

(15) -(CH₂)₀₋₄-CO-R_{N-4} where R_{N-4} is selected from the
group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl,
homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide,
homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is
optionally substituted with one, two, three, or four of: C₁-C₆ alkyl,
(16) -(CH₂)₀₋₄-CO-O-R_{N-5} where R_{N-5} is selected from the group
consisting of:

(a) C₁-C₆ alkyl,

- above,
- (b) $-(CH_2)_{0-2}-(R_{1-aryl})$ where R_{1-aryl} is as defined above,
- bonds,
- (c) C₂-C₆ alkenyl containing one or two double bonds,
- bonds,
- (d) C₂-C₆ alkynyl containing one or two triple bonds,
- (e) C₃-C₇ cycloalkyl,
- (f) $-(CH_2)_{0-2}-(R_{1-heteroaryl})$ where $R_{1-heteroaryl}$ is as defined above,
- (17) $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined above,
- (18) $-(CH_2)_{0-4}-SO-(C_1-C_8 \text{ alkyl})$,
- (19) $-(CH_2)_{0-4}-SO_2-(C_1-C_{12} \text{ alkyl})$,
- (20) $-(CH_2)_{0-4}-SO_2-(C_3-C_7 \text{ cycloalkyl})$,
- (21) $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-O-R_{N-5}$ where R_{N-5} can be the same or different and is as defined above,
- (22) $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-N(R_{N-5})_2$, where R_{N-5} can be the same or different and is as defined above,
- (23) $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$, where R_{N-5} can be the same or different and is as defined above,
- (24) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-CO-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as defined above,
- (25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,
- (26) $-(CH_2)_{0-4}-R_{N-4}$ where R_{N-4} is as defined above,
- (27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$,
- (28) $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$ where $R_{N-aryl-1}$ is -H or C₁-C₄ alkyl,
- (29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$ where R_{N-5} is as defined above,

above,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})_2$ where R_{N-5} is as defined above,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$ where R_{N-5} is as defined above,

above,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})_2$ where R_{N-5} is as defined above,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl}$ optionally substituted with one, two, three, four, or five -F),

(35) C_3-C_7 cycloalkyl,

(36) C_2-C_6 alkenyl with one or two double bonds optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, or -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(37) C_2-C_6 alkynyl with one or two triple bonds optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, or -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(38) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as described above, or

(39) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl,

(B) -R_{N-heteroaryl}, where R_{N-heteroaryl} is selected from the group as defined above in R_{1-heteroaryl} and where the R_{N-heteroaryl} group is bonded by any atom of the parent R_{N-heteroaryl} group substituted by hydrogen such that the new bond to the R_{N-heteroaryl} group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four of:

(1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(2) -OH,

(3) -NO₂,

(4) -F, -Cl, -Br, or -I,

(5) -CO-OH,

(6) -C≡N,

(7) -(CH₂)₀₋₄-CO-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and are selected from the group consisting of:

(a) -H,

(b) -C₁-C₆ alkyl optionally substituted with one substituent selected from the group consisting of:

(i) -OH, and

(ii) -NH₂,

(c) -C₁-C₆ alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,

(d) -C₃-C₇ cycloalkyl,

(e) -(C₁-C₂ alkyl)-(C₃-C₇ cycloalkyl),

(f) -(C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),

(g) -C₂-C₆ alkenyl with one or two double bonds,

(h) -C₂-C₆ alkynyl with one or two triple bonds,

(i) -C₁-C₆ alkyl chain with one double bond and one triple bond,

(j) -R₁-aryl where R₁-aryl is as defined above, and

(k) -R₁-heteroaryl where R₁-heteroaryl is as defined above,

(8) -(CH₂)₀₋₄-CO-(C₁-C₁₂ alkyl),

(9) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkenyl with one, two, or three double bonds),

(10) -(CH₂)₀₋₄-CO-(C₂-C₁₂ alkynyl with one, two, or three triple bonds),

(11) -(CH₂)₀₋₄-CO-(C₃-C₇ cycloalkyl),

(12) -(CH₂)₀₋₄-CO-R₁-aryl where R₁-aryl is as defined above,

(13) -(CH₂)₀₋₄-CO-R₁-heteroaryl where R₁-heteroaryl is as defined above,

(14) -(CH₂)₀₋₄-CO-R₁-heterocycle where R₁-heterocycle is as defined above,

(15) $-(CH_2)_{0-4}-CO-R_{N-4}$ where R_{N-4} is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of: C₁-C₆ alkyl,

(16) $-(CH_2)_{0-4}-CO-O-R_{N-5}$ where R_{N-5} is selected from the group consisting of:

(a) C₁-C₆ alkyl,

(b) $-(CH_2)_{0-2}-(R_{1-aryl})$ where R_{1-aryl} is as defined above,

(c) C₂-C₆ alkenyl containing one or two double bonds,

(d) C₂-C₆ alkynyl containing one or two triple bonds,

(e) C₃-C₇ cycloalkyl, and

(f) $-(CH_2)_{0-2}-(R_{1-heteroaryl})$ where $R_{1-heteroaryl}$ is as defined above,

(17) $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined above,

(18) $-(CH_2)_{0-4}-SO-(C_1-C_8\text{ alkyl}),$

(19) $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}\text{ alkyl}),$

(20) $-(CH_2)_{0-4}-SO_2-(C_3-C_7\text{ cycloalkyl}),$

(21) $-(CH_2)_{0-4}-N(H\text{ or }R_{N-5})-CO-O-R_{N-5}$ where R_{N-5} can be the same or different and is as defined above,

(22) $-(CH_2)_{0-4}-N(H\text{ or }R_{N-5})-CO-N(R_{N-5})_2$, where R_{N-5} can be the same or different and is as defined above,

(23) $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$, where R_{N-5} can be the same or different and is as defined above,

(24) $-(CH_2)_{0-4}-N(-H\text{ or }R_{N-5})-CO-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as defined above,

(25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(26) $-(CH_2)_{0-4}-R_{N-4}$ where R_{N-4} is as defined above,

(27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$,

(28) $-(CH_2)_{0-4}-O-P(O)-(OR_{N-aryl-1})_2$ where $R_{N-aryl-1}$ is $-H$ or C_1-C_4 alkyl,

(29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})_2$ where R_{N-5} is as defined above,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$ where R_{N-5} is as defined above,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})_2$ where R_{N-5} is as defined above,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl}$ optionally substituted with one, two, three, four, or five of $-F$),

(35) C_3-C_7 cycloalkyl,

(36) C_2-C_6 alkenyl with one or two double bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(37) C_2-C_6 alkynyl with one or two triple bonds optionally substituted with C_1-C_3 alkyl, $-F$, $-Cl$, $-Br$, $-I$, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, or

(38) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as described above,

(39) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl,

(C) $R_{N-aryl}-W-R_{N-aryl}$,

(D) $R_{N-aryl}-W-R_{N-heteroaryl}$,

(E) $R_{N-aryl}-W-R_{N-1-heterocycle}$, where $R_{N-1-heterocycle}$ is the same as $R_{1-heterocycle}$, as defined above,

(F) $R_{N-heteroaryl}-W-R_{N-aryl}$,

- (G) $R_{N\text{-heteroaryl}}-W-R_{N\text{-heteroaryl}}$,
- (H) $R_{N\text{-heteroaryl}}-W-R_1\text{-heterocycle}$,
- (I) $R_1\text{-heterocycle}-W-R_{N\text{-aryl}}$,
- (J) $R_1\text{-heterocycle}-W-R_{N\text{-heteroaryl}}$, and
- (K) $R_1\text{-heterocycle}-W-R_1\text{-heterocycle}$,

where W is

- (6) $-(CH_2)_{0-4}-$,
- (7) $-O-$,
- (8) $-S(O)_{0-2}-$,
- (9) $-N(R_{N-5})-$ where R_{N-5} is as defined above, or
- (10) $-CO-$;

(II) $-CO-(C_1-C_{10}\text{ alkyl})$ where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

- (A) $-OH$,
- (B) $-C_1-C_6$ alkoxy,
- (C) $-C_1-C_6$ thioalkoxy,
- (D) $-CO-O-R_{N-8}$ where R_{N-8} is $-H$, C_1-C_6 alkyl or $-phenyl$,
- (E) $-CO-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different

and are as defined above,

- (F) $-CO-R_{N-4}$ where R_{N-4} is as defined above,
- (G) $-SO_2-(C_1-C_8\text{ alkyl})$,
- (H) $-SO_2-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different

and are as defined above,

- (I) $-NH-CO-(C_1-C_6\text{ alkyl})$,
- (J) $-NH-CO-O-R_{N-8}$ where R_{N-8} is as defined above,
- (K) $-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and

are as defined above,

- (L) $-R_{N-4}$ where R_{N-4} is as defined above,
- (M) $-O-CO-(C_1-C_6\text{ alkyl})$,
- (N) $-O-CO-NR_{N-8}R_{N-8}$ where R_{N-8} are the same or different and are

as defined above,

(O) -O-(C₁-C₅ alkyl)-COOH,
(P) -O-(C₁-C₆ alkyl optionally substituted with one, two, or three
-F, -Cl, -Br, or -I),

(Q) -NH-SO₂-(C₁-C₆ alkyl), and
(R) -F, or -Cl,

(III) -CO-(C₁-C₆ alkyl)-O-(C₁-C₆ alkyl) where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

(A) -OH,
(B) -C₁-C₆ alkoxy,
(C) -C₁-C₆ thioalkoxy,
(D) -CO-O-R_{N-8} where R_{N-8} is -H, C₁-C₆ alkyl or -phenyl,
(E) -CO-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different

and are as defined above,

(F) -CO-R_{N-4} where R_{N-4} is as defined above,
(G) -SO₂-(C₁-C₈ alkyl),
(H) -SO₂-NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different

and are as defined above,

(I) -NH-CO-(C₁-C₆ alkyl),
(J) -NH-CO-O-R_{N-8} where R_{N-8} is as defined above,
(K) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are the same or different and

are as defined above,

(L) -R_{N-4} where R_{N-4} is as defined above,
(M) -O-CO-(C₁-C₆ alkyl),
(N) -O-CO-NR_{N-8}R_{N-8} where the R_{N-8}s are the same or different

and are as defined above,

(O) -O-(C₁-C₅ alkyl)-COOH,
(P) -O-(C₁-C₆ alkyl optionally substituted with one, two, or three
-F, -Cl, -Br, or -I),
(Q) -NH-SO₂-(C₁-C₆ alkyl), and
(R) -F, or -Cl,

(IV) $-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})-\text{S}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

- (A) -OH,
- (B) $-\text{C}_1\text{-C}_6$ alkoxy,
- (C) $-\text{C}_1\text{-C}_6$ thioalkoxy,
- (D) $-\text{CO}-\text{O}-\text{R}_{\text{N}-8}$ where $\text{R}_{\text{N}-8}$ is as defined above,
- (E) $-\text{CO}-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$ where $\text{R}_{\text{N}-2}$ and $\text{R}_{\text{N}-3}$ are the same or different

and are as defined above,

- (F) $-\text{CO}-\text{R}_{\text{N}-4}$ where $\text{R}_{\text{N}-4}$ is as defined above,
- (G) $-\text{SO}_2-(\text{C}_1\text{-C}_8 \text{ alkyl})$,
- (H) $-\text{SO}_2-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$ where $\text{R}_{\text{N}-2}$ and $\text{R}_{\text{N}-3}$ are the same or different

and are as defined above,

- (I) $-\text{NH}-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$,
- (J) $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N}-8}$ where $\text{R}_{\text{N}-8}$ is as defined above,
- (K) $-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$ where $\text{R}_{\text{N}-2}$ and $\text{R}_{\text{N}-3}$ are the same or different and

are as defined above,

- (L) $-\text{R}_{\text{N}-4}$ where $\text{R}_{\text{N}-4}$ is as defined above,
- (M) $-\text{O}-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$,
- (N) $-\text{O}-\text{CO}-\text{NR}_{\text{N}-8}\text{R}_{\text{N}-8}$ where $\text{R}_{\text{N}-8}$ are the same or different and are

as defined above,

- (O) $-\text{O}-(\text{C}_1\text{-C}_5 \text{ alkyl})-\text{COOH}$,
- (P) $-\text{O}-(\text{C}_1\text{-C}_6 \text{ alkyl}$ optionally substituted with one, two, or three
-F, -Cl, -Br, or -I),

- (Q) $-\text{NH}-\text{SO}_2-(\text{C}_1\text{-C}_6 \text{ alkyl})$, and

- (R) -F, or -Cl,

(V) $-\text{CO}-\text{CH}(-(\text{CH}_2)_{0-2}-\text{O}-\text{R}_{\text{N}-10})-(\text{CH}_2)_{0-2}-\text{R}_{\text{N-aryl}}/\text{R}_{\text{N-heteroaryl}}$ where $\text{R}_{\text{N-aryl}}$
and $\text{R}_{\text{N-heteroaryl}}$ are as defined above, where $\text{R}_{\text{N}-10}$ is selected from the group consisting of:

- (A) -H,
- (B) $\text{C}_1\text{-C}_6$ alkyl,
- (C) $\text{C}_3\text{-C}_7$ cycloalkyl,
- (D) $\text{C}_2\text{-C}_6$ alkenyl with one double bond,

- (E) C_2-C_6 alkynyl with one triple bond;
- (F) $R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, and
- (G) $R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is as defined above, or
- (VI) $-\text{CO-}(C_3-C_8 \text{ cycloalkyl})$ where alkyl is optionally substituted with one or two substituents selected from the group consisting of:
- (A) $-(\text{CH}_2)_0-4\text{-OH}$,
- (B) $-(\text{CH}_2)_0-4\text{-C}_1\text{-C}_6$ alkoxy,
- (C) $-(\text{CH}_2)_0-4\text{-C}_1\text{-C}_6$ thioalkoxy,
- (D) $-(\text{CH}_2)_0-4\text{-CO-O-R}_{N\text{-8}}$ where $R_{N\text{-8}}$ is $-\text{H}$, $C_1\text{-C}_6$ alkyl or $-\text{phenyl}$,
- (E) $-(\text{CH}_2)_0-4\text{-CO-NR}_{N\text{-2}}\text{R}_{N\text{-3}}$ where $R_{N\text{-2}}$ and $R_{N\text{-3}}$ are the same or different and are as defined above,
- (F) $-(\text{CH}_2)_0-4\text{-CO-R}_{N\text{-4}}$ where $R_{N\text{-4}}$ is as defined above,
- (G) $-(\text{CH}_2)_0-4\text{-SO}_2\text{-}(C_1\text{-C}_8 \text{ alkyl})$,
- (H) $-(\text{CH}_2)_0-4\text{-SO}_2\text{-NR}_{N\text{-2}}\text{R}_{N\text{-3}}$ where $R_{N\text{-2}}$ and $R_{N\text{-3}}$ are the same or different and are as defined above,
- (I) $-(\text{CH}_2)_0-4\text{-NH-CO-(C}_1\text{-C}_6 \text{ alkyl)}$,
- (J) $-\text{NH-CO-O-R}_{N\text{-8}}$ where $R_{N\text{-8}}$ is as defined above,
- (K) $-(\text{CH}_2)_0-4\text{-NR}_{N\text{-2}}\text{R}_{N\text{-3}}$ where $R_{N\text{-2}}$ and $R_{N\text{-3}}$ are the same or different and are as defined above,
- (L) $-(\text{CH}_2)_0-4\text{-R}_{N\text{-4}}$ where $R_{N\text{-4}}$ is as defined above,
- (M) $-\text{O-CO-(C}_1\text{-C}_6 \text{ alkyl)}$,
- (N) $-\text{O-CO-NR}_{N\text{-8}}\text{R}_{N\text{-8}}$ where $R_{N\text{-8}}$ are the same or different and are as defined above,
- (O) $-\text{O-(C}_1\text{-C}_5 \text{ alkyl)-COOH}$,
- (P) $-\text{O-(C}_1\text{-C}_6 \text{ alkyl}$ optionally substituted with one, two, or three $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$),
- (Q) $-\text{NH-SO}_2\text{-}(C_1\text{-C}_6 \text{ alkyl})$, and
- (R) $-\text{F}$, or $-\text{Cl}$;

where R_{N-A} is selected from the group consisting of H, $C_1 - C_{10}$ alkyl, $C_2 - C_{10}$ alkenyl and alkynyl, phenyl, $C_1 - C_4$ alkyl- R_{N-aryl} , $C_1 - C_4$ alkyl- $R_{N-heteroaryl}$, $C_1 - C_4$ alkyl- C_3-C_7 cycloalkyl and $C_1 - C_4$ alkyl- $R_{1-heterocycle}$, wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, C_1-C_3 alkoxy, -C(O)O-R_{1-a}, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H, C_1-C_6 alkyl or phenyl;

where Z is selected from the group consisting of:

- (A) -C(O)-,
- (B) -S(O)₁₋₂-,
- (C) -C(O)-X_{N-1}- where X_{N-1} is selected from the group consisting of -O-, -S- and -NR'- and where R' is as defined above; and
- (D) a single bond;

where R_C is:

(I) - C_1-C_{10} alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O-phenyl, -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -OC=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -S(=O)₀₋₂ R_{1-a} where R_{1-a} is as defined above, -NR_{1-a}C=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, -C=O NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, and -S(=O)₂ NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(II) -(CH₂)₀₋₃-(C₃-C₈) cycloalkyl where cycloalkyl can be optionally substituted with one, two, or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O-phenyl, -CO-OH, -CO-O-(C_1-C_4 alkyl), and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

- (III) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl} where R_{C-x} and R_{C-y} are
 - (H) -H,
 - (I) C_1-C_4 alkyl optionally substituted with one, or two -OH,
 - (J) C_1-C_4 alkoxy optionally substituted with one, two, or three -F,

- (K) -(CH₂)₀₋₄-C₃-C₇ cycloalkyl,
- (L) C₂-C₆ alkenyl containing one or two double bonds,
- (M) C₂-C₆ alkynyl containing one or two triple bonds,
- (N) phenyl-, or
- (B) C₀-C₄ alkyl-C(O) NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

and where R_{C-x} and R_{C-y} are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO₂-, -NR_{N-2}- and R_{C-aryl} where R_{C-aryl} is the same as R_{N-aryl} and where R_{C-aryl} may optionally be substituted with -C₀-C₄ alkyl-C(O) NR_{1-a}R_{1-b}, C₀-C₄ alkyl-C(O) OR_{1-a} where R_{1-a} and R_{1-b} are as defined above,

(IV) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-heteroaryl} where R_{C-heteroaryl} is the same as R_{N-heteroaryl} and R_{C-x} and R_{C-y} are as defined above,

(V) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl}-R_{C-aryl} where R_{C-aryl}, R_{C-x} and R_{C-y} are as defined above,

(VI) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl}-R_{C-heteroaryl} where R_{C-aryl}, R_{C-heteroaryl}, R_{C-x} and R_{C-y} are as defined above,

(VII) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-heteroaryl}-R_{C-aryl} where R_{C-heteroaryl}, R_{C-aryl}, R_{C-x} and R_{C-y} are as defined above,

(VIII) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-heteroaryl}-R_{C-heteroaryl} where R_{C-heteroaryl}, R_{C-x} and R_{C-y} are as defined above,

(IX) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-aryl}-R_{C-heterocycle} where R_{C-heterocycle} is the same as R_{1-heterocycle}, and where R_{C-aryl}, R_{C-x} and R_{C-y} are as defined above,

(X) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-heteroaryl}-R_{C-heterocycle} where R_{C-heteroaryl}, R_{C-heterocycle}, R_{C-x} and R_{C-y} are as defined above,

(XI) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-heterocycle}-R_{C-aryl} where R_{C-heterocycle}, R_{C-aryl}, R_{C-x} and R_{C-y} are as defined above,

(XII) -(CR_{C-x}R_{C-y})₀₋₄-R_{C-heterocycle}-R_{C-heteroaryl} where R_{C-heterocycle}, R_{C-heteroaryl}, R_{C-x} and R_{C-y} are as defined above,

(XIII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}-R_{C-heterocycle}$ where $R_{C-heterocycle}$, R_{C-x} and R_{C-y} are as defined above,

(XIV) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heterocycle}$ where $R_{C-heterocycle}$, R_{C-x} and R_{C-y} are as defined above,

(XV) $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$ where R_{C-3} is as defined below and R_{C-1} , R_{C-2} are the same or different and are selected from the group consisting of:

(A) -H,

(B) $-C_1-C_6$ alkyl, optionally substituted with up to three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(D) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(E) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(F) $-(CH_2)_{1-2}-S(O)_{0-2}-(C_1-C_6$ alkyl),

(F) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

(G) $-(C_1-C_4$ alkyl)- $R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined for R_{1-aryl},

(H) $-(C_1-C_4$ alkyl)- $R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

(I) $-(C_1-C_4$ alkyl)- $R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(J) $-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

(K) $-R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(M) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C'-aryl}$ where R_{C-4} is -O-, -S- or -NR_{C-5}- where R_{C-5} is C_1-C_6 alkyl, and where $R_{C'-aryl}$ is defined above,

(N) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C-heteroaryl}$ where R_{C-4} and $R_{C-heteroaryl}$ are as defined above, and

(O) $-R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above, and where R_{C-3} is the same or different and is:

(A) H,

(B) $-C_1-C_6$ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(C) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(D) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(E) $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF₃, C_1-C_6 alkoxy, -O- phenyl, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(F) $-R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,

(G) $-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

(H) $-R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(I) $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$ where $R_{C'-aryl}$ is as defined above,

(J) $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ is as defined above,

or

(K) $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$ where $R_{C-heterocycle}$ is as defined above,

(XVI) $-CH(R_{C-aryl})_2$ where R_{C-aryl} are the same or different and are as defined above,

(XVII) $-\text{CH}(\text{R}_{\text{C-heteraryl}})_2$ where $\text{R}_{\text{C-heteraryl}}$ are the same or different and are as defined above,

(XVIII) $-\text{CH}(\text{R}_{\text{C-aryl}})(\text{R}_{\text{C-heteraryl}})$ where $\text{R}_{\text{C-aryl}}$ and $\text{R}_{\text{C-heteraryl}}$ are as defined above,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to $\text{R}_{\text{C-aryl}}$ or $\text{R}_{\text{C-heteraryl}}$ or $\text{R}_{\text{C-heterocycle}}$ where $\text{R}_{\text{C-aryl}}$ or $\text{R}_{\text{C-heteraryl}}$ or $\text{R}_{\text{C-heterocycle}}$ are as defined above where one carbon of cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with NH, $\text{NR}_{\text{N-5}}$, O, or $\text{S}(=\text{O})_{0-2}$, and where cyclopentyl, cyclohexyl, or cycloheptyl can be optionally substituted with one or two $\text{C}_1\text{-C}_3$ alkyl, -F, -OH, -SH, $-\text{C}\equiv\text{N}$, $-\text{CF}_3$, $\text{C}_1\text{-C}_6$ alkoxy, =O, or $-\text{NR}_{1-a}\text{R}_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(XX) $\text{C}_2\text{-C}_{10}$ alkenyl containing one or two double bonds optionally substituted with one, two or three substituents selected from the group consisting of $\text{C}_1\text{-C}_3$ alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-\text{C}\equiv\text{N}$, $-\text{CF}_3$, $\text{C}_1\text{-C}_6$ alkoxy, -O- phenyl, and $-\text{NR}_{1-a}\text{R}_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(XXI) $\text{C}_2\text{-C}_{10}$ alkynyl containing one or two triple bonds optionally substituted with one, two or three substituents selected from the group consisting of $\text{C}_1\text{-C}_3$ alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-\text{C}\equiv\text{N}$, $-\text{CF}_3$, $\text{C}_1\text{-C}_6$ alkoxy, -O- phenyl, and $-\text{NR}_{1-a}\text{R}_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(XXI) $-(\text{CH}_2)_{0-1}\text{-CHR}_{\text{C-6}}\text{-}(\text{CH}_2)_{0-1}\text{-R}_{\text{C-aryl}}$ where $\text{R}_{\text{C-aryl}}$ is as defined above and $\text{R}_{\text{C-6}}$ is $-(\text{CH}_2)_{0-6}\text{-OH}$,

(XXII) $-(\text{CH}_2)_{0-1}\text{-CHR}_{\text{C-6}}\text{-}(\text{CH}_2)_{0-1}\text{-R}_{\text{C-heteraryl}}$ where $\text{R}_{\text{C-heteraryl}}$ and $\text{R}_{\text{C-6}}$ is as defined above,

(XXIII) $-\text{CH}(-\text{R}_{\text{C-aryl}} \text{ or } \text{R}_{\text{C-heteraryl}})\text{-CO-O(C}_1\text{-C}_4\text{ alkyl)}$ where $\text{R}_{\text{C-aryl}}$ and $\text{R}_{\text{C-heteraryl}}$ are as defined above,

(XXIV) $-\text{CH}(-\text{CH}_2\text{-OH})\text{-CH}(-\text{OH})\text{-phenyl-NO}_2$,

(XXV) $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-O-(C}_1\text{-C}_6 \text{ alkyl)-OH}$,

(XXVII) $-\text{CH}_2\text{-NH-CH}_2\text{-CH}(-\text{O-CH}_2\text{-CH}_3)_2$, or

(XXVIII) $-(\text{CH}_2)_{0-6}\text{-C(=NR}_{1-a}\text{)(NR}_{1-a}\text{R}_{1-b})$ where R_{1-a} and R_{1-b} are as defined above,

where R_{C-A} is H, $C_1 - C_{10}$ alkyl, $C_2 - C_{10}$ alkenyl and alkynyl, phenyl, $C_1 - C_4$ alkyl- R_{N-aryl} , $C_1 - C_4$ alkyl- $R_{N-heteroaryl}$, $C_1 - C_4$ alkyl-C3-C7 cycloalkyl, or $C_1 - C_4$ alkyl- $R_{1-heterocycle}$, wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1 - C_3$ alkoxy, -C(O)O- R_{1-a} , and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H, $C_1 - C_6$ alkyl or phenyl;

where R_{C-A} , -Z- R_C , and the nitrogen atom to which they attach may cyclize to form a ring or fused rings chosen from the group consisting of 5-8 membered heterocyclics having up to 2 heteroatoms in addition to the ring nitrogen defined above chosen from the group consisting of N, O, and S, which may optionally be fused with one, or two phenyl, pyridyl, cyclohexyl, piperidinyl or morpholinyl,

where the ring or fused rings may optionally have one, two, or three substituents independently chosen from the group of:

(1) $C_1 - C_6$ alkyl,

$C_2 - C_6$ alkenyl with one or two double bonds, or

$C_2 - C_6$ alkynyl with one or two triple bonds, wherein each may be optionally substituted with one, two, or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF₃, $C_1 - C_3$ alkoxy, and -NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are -H or $C_1 - C_6$ alkyl,

(10) -F, Cl, -Br, or -I,

(11) - $C_1 - C_6$ alkoxy optionally substituted with one, two, or three -F,

(12) -NR_{N-2}R_{N-3} where R_{N-2} and R_{N-3} are as defined below,

(13) -OH,

(14) -C≡N,

(15) =O (oxo),

(16) -CO-($C_1 - C_4$ alkyl),

(17) -SO₂-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above, or

(18) -CO-NR_{1-a}R_{1-b} where R_{1-a} and R_{1-b} are as defined above,

or pharmaceutically acceptable salts thereof.

65. A method of treatment according to claim 64, wherein the disease is Alzheimer's disease.
66. A method of treatment according to claim 64, wherein the method is helping prevent or delay the onset of Alzheimer's disease.
67. A method of treatment according to claim 64, wherein the disease is mild cognitive impairment.
68. A method of treatment according to claim 64, wherein the disease is Down's syndrome.
69. A method of treatment according to claim 64, wherein the disease is Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type.
70. A method of treatment according to claim 64, wherein the disease is cerebral amyloid angiopathy.
71. A method of treatment according to claim 64, wherein the disease is degenerative dementias.
72. A method of treatment according to claim 64, wherein the disease is diffuse Lewy body type of Alzheimer's disease.
73. A method of treatment according to claim 64, wherein the method is treating an existing disease.
74. A method of treatment according to claim 64, wherein the method is preventing a disease from developing.

75. A method of treatment according to claim 64, wherein the therapeutically effective amount for oral administration is from about 0.1 mg/day to about 1,000 mg/day; for parenteral, sublingual, intranasal, intrathecal administration is from about 0.5 to about 100 mg/day; for depo administration and implants is from about 0.5 mg/day to about 50 mg/day; for topical administration is from about 0.5 mg/day to about 200 mg/day; for rectal administration is from about 0.5 mg to about 500 mg.

76. A method of treatment according to claim 75, wherein the therapeutically effective amount for oral administration is from about 1 mg/day to about 100 mg/day and for parenteral administration is from about 5 to about 50 mg daily.

77. A method of treatment according to claim 76 where the therapeutically effective amount for oral administration is from about 5 mg/day to about 50 mg/day.

78. A method of treatment according to claim 64, wherein R₁ is:

- $(CH_2)_{0-1}-(R_{1-aryl})$, or
- $(CH_2)_{n1}-(R_{1-heteroaryl})$.

79. A method of treatment according to claim 78, wherein R₁ is:

- $(CH_2)-(R_{1-aryl})$, or
- $(CH_2)-(R_{1-heteroaryl})$.

80. A method of treatment according to claim 79, wherein R₁ is - $(CH_2)-(R_{1-aryl})$ where R_{1-aryl} is phenyl.

81. A method of treatment according to claim 80, wherein R₁ is substituted with two -F.

82. A method of treatment according to claim 81, wherein the -F substitutions are on the -3 and -5 positions.

83. A method of treatment according to claim 64, wherein R₂ and R₃ are both -H.

84. A method of treatment according to claim 64, wherein R_C is:

- C₁-C₈ alkyl,
- (CH₂)₀₋₃-(C₃-C₇) cycloalkyl,
- (CR_{C-x}R_{C-y})₀₋₄-R_C-aryl,
- (CR_{C-x}R_{C-y})₀₋₄-R_C-heteroaryl,
- (CR_{C-x}R_{C-y})₀₋₄-R_C-heterocycle, or
- cyclopentyl or -cyclohexyl ring fused to R_C-aryl or R_C-heteroaryl or R_C-heterocycle.

85. A method of treatment according to claim 84, wherein R_C is:

- (CH₂)₀₋₃-(C₃-C₇) cycloalkyl,
- (CR_{C-x}R_{C-y})₀₋₄-R_C-aryl,
- (CR_{C-x}R_{C-y})₀₋₄-R_C-heteroaryl,
- (CR_{C-x}R_{C-y})₀₋₄-R_C-heterocycle,
- cyclopentyl or -cyclohexyl ring fused to a R_C-aryl or R_C-heteroaryl or R_C-heterocycle.

86. A method of treatment according to claim 85, wherein R_C is:

- (CR_{C-x}R_{C-y})₀₋₄-R_C-aryl,
- (CR_{C-x}R_{C-y})₀₋₄-R_C-heteroaryl,
- cyclopentyl or -cyclohexyl ring fused to a R_C-aryl or R_C-heteroaryl or R_C-heterocycle.

87. A method of treatment according to claim 86, wherein R_C is:

- (CR_{C-x}R_{C-y})₀₋₄-R_C-aryl where R_C-aryl is phenyl.

88. A method of treatment according to claim 87, wherein said phenyl is substituted in the 3-position or 3,5-positions.

89. A method of treatment according to claim 64, wherein R_{C-A} is:

- methyl, or
- ethyl.

90. A method of treatment according to claim 64, wherein Z is:
-C(O)-, or
-C(Q)-X_{N-1}- where X_{N-1} is selected from the group consisting of -O-, -S- and -NR'-.
91. A method of treatment according to claim 64, wherein R_N is:
-R_{N-1}-X_N- where X_N is -CO-, where R_{N-1} is R_N-aryl or R_N-heteroaryl where R_N-aryl is phenyl where the substitution on phenyl is 1,3-, and where R_N-aryl or R_N-heteroaryl are substituted with one -CO-NR_{N-2}R_{N-3},
-R_{N-1}-X_N- where X_N is -CO-, where R_{N-1} is R_N-aryl or R_N-heteroaryl where R_N-aryl is phenyl substituted with one C₁ alkyl where the substitution on the phenyl is 1,3,5-, and where R_N-aryl or R_N-heteroaryl are substituted with one -CO-NR_{N-2}R_{N-3}, or
-R_{N-1}-X_N- where X_N is -CO-, where R_{N-1} is R_N-heteroaryl where R_N-heteroaryl is substituted with one -CO-NR_{N-2}R_{N-3}.
92. A method of treatment according to claim 91, wherein R_{N-2} and R_{N-3} are the same and are C₃ alkyl.
93. A method of treatment according to claim 91, wherein R_{N-1}-X_N- where X_N is -CO-, where R_{N-1} is R_N-aryl where R_N-aryl is phenyl substituted with one -CO-NR_{N-2}R_{N-3} where the substitution on phenyl is 1,3-.
94. A method of treatment according to claim 91, wherein R_{N-1}-X_N- where X_N is -CO-, where R_{N-1} is R_N-aryl where R_N-aryl is phenyl substituted with one C₁ alkyl and with one -CO-NR_{N-2}R_{N-3} where the substitution on the phenyl is 1,3,5-.
95. A method of treatment according to claim 91, wherein X_N is -CO- , or -SO₂-.
96. A method of treatment according to claim 95, wherein X_N is -CO-.

97. A method of treatment according to claim 64 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids: acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate, camsylic, carbonic, chlorobenzoic, citric, edetic, edisyllic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycolylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

98. A method of treatment according to claim 36 or 64 where the disubstituted amine is selected from the group consisting of:

6-({[(2S,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]benzoyl} amino)-2-hydroxybutyl](ethyl)amino]carbonyl} amino)hexanoic acid,
N¹-((1S,2S)-1-(3,5-difluorobenzyl)-3-{ethyl[(isobutylamino)carbonyl]amino}-2-hydroxypropyl)-N³,N³-dipropylisophthalamide,
N¹-[(1S,2S)-3-[(butylsulfonyl)(ethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N³,N³-dipropylisophthalamide,
N¹-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{(2S)-2-[(isobutylamino)carbonyl]piperidinyl} propyl)-5-methyl-N³,N³-dipropylisophthalamide,
N¹-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(4-methyl-1-piperazinyl)propyl]-5-methyl-N³,N³-dipropylisophthalamide,,
N¹-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[2-(isobutylamino)-2-oxoethyl](methyl)amino]propyl}-5-methyl-N³,N³-dipropylisophthalamide,
N¹-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-2-(isobutylamino)-1-methyl-2-oxoethyl](methyl)amino]propyl}-5-methyl-N³,N³-dipropylisophthalamide,
N¹-[(1S,2R)-1-benzyl-2-hydroxy-3-(1,3-thiazolidin-3-yl)propyl]-N³,N³-dipropylisophthalamide, and

~~N¹-{(1S,2R)-1-benzyl-3-[4-(4-fluorophenyl)-1-piperazinyl]-2-hydroxypropyl}-N³,N³-dipropylisophthalamide.~~

99. A method for inhibiting beta-secretase activity, comprising exposing said beta-secretase to an effective inhibitory amount of a compound according to claim ~~1~~.

100. The method of claim 99, wherein said beta-secretase is exposed to said compound *in vitro*.

101. The method of claim 99, wherein said beta-secretase is exposed to said compound in a cell.

102. The method of claim 101, wherein said cell is in an animal.

103. The method of claim 102, wherein said animal is a human.

104. A method for inhibiting beta-secretase activity, comprising exposing said beta-secretase to an effective inhibitory amount of a compound according to claim ~~15~~.

105. The method of claim 104, wherein said beta-secretase is exposed to said compound *in vitro*.

106. The method of claim 104, wherein said beta-secretase is exposed to said compound in a cell.

107. The method of claim 106, wherein said cell is in an animal.

108. The method of claim 107, wherein said animal is a human.

109. The method of claims 99 or 104, wherein the compound is selected from the group consisting of:

6-({[(2S,3S)-4-(3,5-difluorophenyl)-3-{(3-
[(dipropylamino)carbonyl]benzoyl}amino)-2-
hydroxybutyl](ethyl)amino]carbonyl}amino)hexanoic acid,
N¹-((1S,2S)-1-(3,5-difluorobenzyl)-3-{ethyl[(isobutylamino)carbonyl]amino}-2-
hydroxypropyl)-N³,N³-dipropylisophthalamide,
N¹-[(1S,2S)-3-[(butylsulfonyl)(ethyl)amino]-1-(3,5-difluorobenzyl)-2-
hydroxypropyl]-5-methyl-N³,N³-dipropylisophthalamide,
N¹-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{(2S)-2-
[(isobutylamino)carbonyl]piperidinyl}propyl)-5-methyl-N³,N³-dipropylisophthalamide,
N¹-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(4-methyl-1-
piperazinyl)propyl]-5-methyl-N³,N³-dipropylisophthalamide,,
N¹-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[2-(isobutylamino)-2-
oxoethyl](methyl)amino]propyl}-5-methyl-N³,N³-dipropylisophthalamide,
N¹-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-2-(isobutylamino)-1-
methyl-2-oxoethyl](methyl)amino]propyl}-5-methyl-N³,N³-dipropylisophthalamide,
N¹-[(1S,2R)-1-benzyl-2-hydroxy-3-(1,3-thiazolidin-3-yl)propyl]-N³,N³-
dipropylisophthalamide, and
N¹-{(1S,2R)-1-benzyl-3-[4-(4-fluorophenyl)-1-piperazinyl]-2-hydroxypropyl}-
N³,N³-dipropylisophthalamide.

110. A method for inhibiting cleavage of amyloid precursor protein (APP), in a reaction mixture, at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a compound according to claim

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111. The method of claim 110, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the APP-770 isotype; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.

112. The method of claim 110, wherein said reaction mixture is exposed *in vitro*.
113. The method of claim 110, wherein said reaction mixture is exposed in a cell.
114. The method of claim 113, wherein said cell is an animal cell.
115. The method of claim 114, wherein said cell is a human cell.
116. A method for inhibiting cleavage of amyloid precursor protein (APP), in a reaction mixture, at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a compound according to claim 15.
117. The method of claim 116, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the APP-770 isotype; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.
118. The method of claim 116, wherein said reaction mixture is exposed *in vitro*.
119. The method of claim 116, wherein said reaction mixture is exposed in a cell.
120. The method of claim 118, wherein said cell is an animal cell.
121. The method of claim 120, wherein said cell is a human cell.

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122. A method for inhibiting production of amyloid beta peptide (A beta) in a cell, comprising administering to said cell an effective inhibitory amount of a compound according to claim 1.

123. The method of claim 122, wherein said administering is to an animal.

124. The method of claim 123, wherein said administering is to a human.

125. A method for inhibiting production of amyloid beta peptide (A beta) in a cell, comprising administering to said cell an effective inhibitory amount of a compound according to claim 15.

126. The method of claim 125, wherein said administering is to an animal.

127. The method of claim 126, wherein said administering is to a human.

128. A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibitory amount of a compound according to claim 1.

129. The method of claim 128, wherein said animal is a human.

130. A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibitory amount of a compound according to claim 15.

131. The method of claim 130, wherein said animal is a human.

132. A method for treating or preventing a disease characterized by beta-amyloid deposits in the brain comprising administering to a patient an effective therapeutic amount of a compound according to claim 1.

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133. The method of claim 132, wherein said therapeutic amount is in the range of from about 0.1 to about 1000 mg/day.

134. The method of claim 132, wherein said therapeutic amount is in the range of from about 15 to about 1500 mg/day.

135. The method of claim 133, wherein said therapeutic amount is in the range of from about 1 to about 100 mg/day.

136. The method of claim 135, wherein said therapeutic amount is in the range of from about 5 to about 50 mg/day.

137. The method of claim 133, wherein said disease is Alzheimer's disease.

138. The method of claim 132, wherein said disease is Mild Cognitive Impairment, Down's Syndrome, or Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch Type.

139. A method for treating or preventing a disease characterized by beta-amyloid deposits in the brain comprising administering to a patient an effective therapeutic amount of a compound according to claim 15.

140. The method of claim 139, wherein said therapeutic amount is in the range of from about 0.1 to about 1000 mg/day.

141. The method of claim 139, wherein said therapeutic amount is in the range of from about 15 to about 1500 mg/day.

142. The method of claim 140, wherein said therapeutic amount is in the range of from about 1 to about 100 mg/day.

143. The method of claim 142, wherein said therapeutic amount is in the range of from about 5 to about 50 mg/day.

144. The method of claim 139, wherein said disease is Alzheimer's disease.

145. The method of claim 139, wherein said disease is Mild Cognitive Impairment, Down's Syndrome, or Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch Type.

Sub A1
146. A composition comprising beta-secretase complexed with a compound according to claim 1.

147. A composition comprising beta-secretase complexed with a compound according to claim 15.

Sub A1
148. A method for producing a beta-secretase complex comprising: exposing beta-secretase to a compound according to claim 1, or a pharmaceutically acceptable salt thereof in a reaction mixture under conditions suitable for the production of said complex.

149. The method of claim 148, where said exposing is *in vitro*.

150. The method of claim 149, wherein said reaction mixture is a cell.

151. A method for producing a beta-secretase complex comprising: exposing beta-secretase to a compound according to claim 15, or a pharmaceutically acceptable salt thereof in a reaction mixture under conditions suitable for the production of said complex.

152. The method of claim 151, where said exposing is *in vitro*.

153. The method of claim 152, wherein said reaction mixture is a cell.
154. A kit comprising component parts capable of being assembled, wherein at least one component part comprises a compound according to claim 1, enclosed in a container.
155. The kit of claim 154, wherein said compound is lyophilized and at least one further component part comprises a diluent.
156. A kit comprising component parts capable of being assembled, wherein at least one component part comprises a compound according to claim 15, enclosed in a container.
157. The kit of claim 156, wherein said compound is lyophilized and at least one further component part comprises a diluent.
158. A kit comprising a plurality of containers, each container comprising one or more unit dose of a compound according to claim 1.
- A1 159. The kit of claim 158, wherein each container is adapted for oral delivery and comprises a tablet, gel, or capsule.
160. The kit of claim 158, wherein each container is adapted for parenteral delivery and comprises a depot product, syringe, ampoule, or vial.
161. The kit of claim 158, wherein each container is adapted for topical delivery and comprises a patch, medipad, ointment, or cream.
162. A kit comprising a plurality of containers, each container comprising one or more unit dose of a compound according to claim 1.

163. The kit of claim 162, wherein each container is adapted for oral delivery and comprises a tablet, gel, or capsule.
164. The kit of claim 162, wherein each container is adapted for parenteral delivery and comprises a depot product, syringe, ampoule, or vial.
165. The kit of claim 162, wherein each container is adapted for topical delivery and comprises a patch, medipad, ointment, or cream.
166. A kit comprising a compound according to claim 1; and one or more therapeutic agent selected from the group consisting of an antioxidant, an anti-inflammatory, a gamma secretase inhibitor, a neurotrophic agent, an acetylcholinesterase inhibitor, a statin, an A beta peptide, and an anti-A beta antibody.
167. A kit comprising a compound according to claim 15; and one or more therapeutic agent selected from the group consisting of an antioxidant, an anti-inflammatory, a gamma secretase inhibitor, a neurotrophic agent, an acetylcholinesterase inhibitor, a statin, an A beta peptide, and an anti-A beta antibody.
168. A composition comprising a compound according to claim 1; and an inert diluent or edible carrier.
169. The composition of claim 168, wherein said carrier is an oil.
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170. A composition comprising a compound according to claim 1; and an inert diluent or edible carrier.
171. The composition of claim 170, wherein said carrier is an oil.
172. A composition comprising a compound according to claim 1; and a binder, excipient, disintegrating agent, lubricant, or gildant.

173. A composition comprising a compound according to claim 15; and a binder, excipient, disintegrating agent, lubricant, or gildant.
174. A composition comprising a compound according to claim 1 disposed in a cream, ointment, or patch.
175. A composition comprising a compound according to claim 15 disposed in a cream, ointment, or patch.

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